RISK EVALUATION AND MITIGATION STRATEGY (REMS)

The iPLEDGE Program

Single Shared System for Isotretinoin
1. **GOALS**

   The goals of the isotretinoin risk evaluation and mitigation strategy are:

   1. To prevent fetal exposure to isotretinoin
   2. To inform prescribers, pharmacists, and patients about isotretinoin’s serious risks and safe-use conditions

2. **REMS ELEMENTS**

2.1. **Medication Guide**

A Medication Guide for isotretinoin is dispensed with each prescription for isotretinoin in accordance with 21 CFR 208.24, as described below.

A Medication Guide is enclosed with each blister package of isotretinoin to ensure that the Medication Guide is given to each patient with each prescription.

The currently approved isotretinoin Medication Guide is part of this REMS.

2.2. **Elements to Assure Safe Use**

2.2.1. **Healthcare providers who prescribe isotretinoin are specially certified in the iPLEDGE Program.**

   a. Isotretinoin sponsors will ensure that healthcare providers who prescribe isotretinoin are specially certified in the iPLEDGE Program. To become certified, each prescriber must activate registration, by completing the Prescriber Enrollment Form, via the iPLEDGE Program website or the automated phone system. The registration and activation requires each prescriber to agree to do the following:

      i. Register each patient in the iPLEDGE Program via the iPLEDGE Program website or automated phone system.
      ii. Understands the risks of fetal exposure to isotretinoin and the risk factors for unplanned pregnancy.
      iii. Correctly identify and document patients as females of reproductive potential, females of non-reproductive potential, or males.
      iv. Provide contraception counseling to females of reproductive potential prior to and during isotretinoin treatment, or refer females of reproductive potential to an expert for such counseling.
v. Provide scheduled pregnancy testing for females of reproductive potential and then verify and document the negative pregnancy test result prior to writing each prescription.

vi. Document the two chosen forms of contraception for each female of reproductive potential prior to writing each prescription.

vii. Prescribe no more than a 30-day supply of isotretinoin with no refills.

viii. Report any pregnancies in patients prescribed isotretinoin to the iPLEDGE Program.

b. Isotretinoin sponsors will ensure the iPLEDGE Program documents that certified prescribers/designees have performed the following responsibilities prior to initiating isotretinoin treatment and monthly prior to providing each prescription:

i. Counseled the patient about isotretinoin risks.

ii. Determined the reproductive status of all female patients prior to initiating treatment, and determined whether the reproductive status of female patients has changed.

iii. For patients who are females of reproductive potential, provide evidence or other documentation that prescribers/designees have:

   a. Obtained a negative CLIA-certified pregnancy test result.
   b. Determined that each female of reproductive potential has appropriate contraception and has been re-counseled about the importance of complying with contraceptive methods.

c. Isotretinoin sponsors will:

i. Maintain a validated and secure database of all iPLEDGE Program registered and activated prescribers, designees, and delegates.

ii. Monitor to ensure that only iPLEDGE Program certified prescribers are prescribing isotretinoin.

iii. Monitor to ensure that iPLEDGE Program certified prescribers correctly identify patients who are females of reproductive potential. A female of reproductive potential is defined as a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or medically documented ovarian failure. This definition includes a young woman who has not yet started menstruating.

iv. Monitor certified prescriber compliance with the iPLEDGE Program. Certified prescriber compliance with the iPLEDGE Program includes categorizing female patient risk (females of reproductive potential vs. females of non-reproductive potential), providing counseling as required, documenting contraception forms as required, and providing pregnancy testing for all females of reproductive potential treated with isotretinoin.
v. Institute appropriate corrective action according to the Non-Compliance Action Policy if the prescriber is found to be non-compliant with the iPLEDGE Program.

d. The following materials are part of the REMS and are appended:

i. The Guide to Best Practices For the iPLEDGE Program

ii. Prescriber Contraception Counseling Guide

iii. DVDs for prescriber use in patient counseling: Be Prepared, Be Protected and Be Aware: The Risk of Pregnancy While on Isotretinoin.

iv. Recognizing Psychiatric Disorders In Adolescents And Young Adults

v. Request for Exemption for Patients with Serious Medical Reasons

vi. Office Staff Designee Registration/Activation Form

vii. Instructions for Managing Office Staff Designees

viii. Prescriber Enrollment Form

2.2.2. Isotretinoin will only be dispensed by pharmacies that are specially certified in the iPLEDGE Program.

a. Isotretinoin sponsors will ensure isotretinoin is only dispensed by pharmacies that are certified. To become certified, the pharmacy must become registered and activated in the iPLEDGE Program. To become registered and activated, each pharmacy must identify a “responsible site pharmacist” who completes the Pharmacy Enrollment Form and agrees to do the following before dispensing an isotretinoin prescription:

i. Affirm that all pharmacists will comply with all iPLEDGE Program requirements:

1. Know the risk and severity of fetal injury/birth defects caused by isotretinoin.
2. Dispense only FDA-approved isotretinoin products and obtain isotretinoin only from the iPLEDGE Program registered wholesalers.
3. Do not sell, borrow, loan, or otherwise transfer isotretinoin in any manner to or from another pharmacy.
4. Dispense only to qualified patients determined via authorization from the iPLEDGE Program.
5. Document the Risk Management Authorization (RMA) number on each prescription.
6. Dispense no more than a 30-day supply (no refills).
7. Dispense the isotretinoin Medication Guide with each prescription.
8. Dispense prior to the “do not dispense to a patient after” date provided by the iPLEDGE Program.
9. Return to the manufacturer (or delegate) any unused product if registration is revoked or if the pharmacy chooses to not reactivate.

ii. A pharmacy that has a pharmacy management system
1. that supports electronic telecommunication verification with the iPLEDGE Program system must:
   a) ensure the pharmacy enables its pharmacy management system to support communication with the iPLEDGE Program system, using established telecommunication standards, and runs the standardized validation test transaction to validate the system enhancements.
   b) dispense isotretinoin to patients only after obtaining authorization by processing the prescription through its pharmacy management system to electronically:
      i) verify the prescriber is certified and the patient is enrolled in the iPLEDGE Program prior to dispensing isotretinoin.
      ii) verify the patient is qualified to receive isotretinoin via receipt of a Risk Management Authorization (RMA) number from the iPLEDGE Program prior to dispensing isotretinoin.

2. that does not support electronic telecommunication verification with the iPLEDGE Program system must:
   a) Dispense isotretinoin to patients only after obtaining authorization by iPLEDGE Program’s web- or voice-based system to:
      i) Verify the prescriber is certified and the patient is enrolled in the iPLEDGE REMS Program
      ii) Verify the patient is qualified to receive isotretinoin via receipt of a Risk Management Authorization (RMA) number from the iPLEDGE Program prior to dispensing isotretinoin

iii. Re-activate pharmacy iPLEDGE Program registration annually.

b. The following materials are part of the REMS and are appended:
   i. Pharmacist Guide for the iPLEDGE Program
   ii. Pharmacy Enrollment Form

2.2.3. Isotretinoin sponsors will ensure that isotretinoin will only be dispensed to patients enrolled in the iPLEDGE Program with evidence or other documentation of safe-use conditions.

a. Isotretinoin sponsors will ensure that all patients treated with isotretinoin are enrolled in the iPLEDGE Program by a registered prescriber, before isotretinoin is
dispensed to them. To become enrolled, each patient or guardian must sign the appropriate Patient Information/Informed Consent form acknowledging that:

i. He or she understands the potential fetal harm with female patient exposure to isotretinoin.

ii. Enrollment in the iPLEDGE Program is required.

iii. Isotretinoin must not be shared with anyone, even someone with similar symptoms.

iv. He or she cannot donate blood while on isotretinoin and for 1 month after treatment has ended.

v. He or she must obtain the prescription within specified time frames.

b. Isotretinoin sponsors must ensure that isotretinoin is dispensed to females of reproductive potential only if there is evidence or other documentation that they meet the following safe-use conditions:

i. Are not pregnant or breastfeeding.

ii. Comply with the required pregnancy testing as ordered by the certified prescriber before receiving each isotretinoin prescription follows:

   1. Two urine or serum pregnancy tests before receiving the initial isotretinoin prescription. The screening test and confirmation test must be at least 19 days apart. For patients with regular menstrual cycles, the confirmation test should be done during the first 5 days of the menstrual period immediately preceding treatment. For patients with amenorrhea, irregular cycles, or using contraceptive methods that preclude withdrawal bleeding, the confirmation test must be immediately preceding treatment and at least 19 days after the screening test.

   2. Monthly pregnancy testing done prior to receiving authorization to receive each isotretinoin prescription.

iii. Unless continuously abstinent, comply with the iPLEDGE Program requirement to use 2 forms of contraception 1 month before, during, and for 1 month after discontinuing isotretinoin treatment.

iv. Access the iPLEDGE Program system before receiving each isotretinoin prescription and 1 month after isotretinoin treatment concludes to answer questions about the program requirements and to enter 2 chosen forms of contraception.

v. Be informed of the purpose and importance of providing information about her pregnancy, should she become pregnant while taking, or within 1 month of the last dose of isotretinoin.

vi. Be informed of the need to immediately stop isotretinoin treatment if she engages in unprotected heterosexual intercourse.
c. Isotretinoin sponsors will ensure that there is evidence or other documentation that all iPLEDGE Program safe use requirements have been met for each female of reproductive potential prior to receiving isotretinoin each month:

   i. The patient is registered in the iPLEDGE Program and had required pregnancy test(s).
   ii. The patient entered their two chosen forms of birth control into the iPLEDGE Program.
   iii. The patient answered the required questions about the iPLEDGE Program and pregnancy prevention.
   iv. The prescriber entered into the iPLEDGE Program the two chosen forms of contraception after re-counseling.
   v. The patient has a negative pregnancy test result entered into the iPLEDGE Program by the prescriber or designee.

d. The following materials are part of the REMS and are appended:

   i. Guide to Isotretinoin for Female Patients Who Can Get Pregnant
   ii. Guide to Isotretinoin for Male Patients and Female Patients who Cannot Get Pregnant
   iii. The iPLEDGE Program Patient Introductory Brochure
   iv. Isotretinoin Educational Kit for Males and Females of Non-Reproductive Potential
   v. Isotretinoin Educational Kit for Females of Reproductive Potential
   vi. Patient Information/Informed Consent for all patients
   vii. Patient Information/Informed Consent for Females of Reproductive Potential
   viii. Patient Monthly Comprehension Questions

2.2.4 Isotretinoin sponsors will maintain a centralized pregnancy registry for the iPLEDGE Program enrolled female patients who become pregnant and consent to participate in a root cause analysis.

The primary objectives of the iPLEDGE Program Pregnancy Registry are to:

   a. Determine isotretinoin exposure status for each reported pregnancy.
   b. Document the outcome of each isotretinoin exposed pregnancy.
   c. Determine, document, and analyze causes contributing to fetal exposure (root cause analysis).

2.3. Implementation System
The implementation system will include the following:

a. Isotretinoin sponsors will maintain a secure web- and voice-based interface for all certified entities as described in Sections 2.2.2 and 2.2.3. This includes a system and process to monitor pregnancy testing results, and to link monthly prescription authorization (risk management authorization) to collection of the following data:

   i. Patient age, gender, and risk category
   ii. Required counseling
   iii. Prescription data (RMA numbers, dates prescription filled, quantities dispensed)
   iv. For female patients of reproductive potential:
      a. Baseline and monthly pregnancy tests, including 30 day post-therapy test (dates and results)
      b. Chosen methods of contraception
      c. Answers to monthly comprehension questions

v. For females who become pregnant:
   a. Maternal and fetal outcome
   b. Information from the prescriber about circumstances contributing to the fetal exposure

b. Isotretinoin sponsors will monitor wholesaler distribution data to ensure that only registered entities distribute isotretinoin. Wholesalers who distribute isotretinoin must be registered with the iPLEDGE Program prior to distributing isotretinoin and must re-register annually thereafter. Wholesalers must register with the iPLEDGE Program by signing and returning the iPLEDGE Program wholesaler agreement. By signing the agreement, wholesalers affirm that they will comply with all of the following iPLEDGE Program requirements:

   i. Distribute only FDA-approved isotretinoin product
   ii. Only ship isotretinoin to: 1) wholesalers registered in the iPLEDGE Program with prior written consent from the manufacturer; and 2) pharmacies licensed in the US and registered and activated in the iPLEDGE Program.
   iii. Notify the isotretinoin manufacturer (or delegate) of any unregistered and/or non-activated pharmacy or unregistered wholesaler that attempts to order isotretinoin.
   iv. Return to the manufacturer (or delegate) any undistributed product if registration is revoked by the manufacturer or if the wholesaler chooses to not re-register annually.

c. Isotretinoin sponsors will maintain a secure database of all certified pharmacies to ensure compliance with the following:
i. Obtain isotretinoin only from registered wholesalers.

ii. Dispense isotretinoin to patients only after receiving iPLEDGE Program authorization each month for each prescription.

iii. Fill isotretinoin within the allowed timeframes only.

d. Isotretinoin sponsors shall develop and implement a single Non-Compliance Action Policy for handling noncompliant stakeholders.

e. Isotretinoin sponsors will monitor registered wholesaler and certified pharmacy compliance, address deviations, and institute appropriate corrective actions according to the Non-Compliance Action Policy if the wholesaler/pharmacy is found to be non-compliant with the iPLEDGE Program.

f. Isotretinoin sponsors will monitor the internet to ensure isotretinoin is not prescribed, dispensed, or otherwise obtained through the internet or any other means outside of the iPLEDGE Program.

g. Based on monitoring and evaluation of the REMS elements to assure safe use, isotretinoin sponsors will take reasonable steps to work to improve implementation of these elements, as applicable.

h. Isotretinoin sponsors will maintain a call center to support prescribers, patients and pharmacies in interfacing with the iPLEDGE Program.

i. The following materials are part of the REMS and are appended:
   i. iPLEDGE Program wholesaler agreement
   ii. Wholesaler to wholesaler shipment request form

2.4. **Timetable for Submission of Assessments (Applicable only to drugs with an approved new drug application (NDA))**

The iPLEDGE Program assessments will be submitted to FDA on May 1, 2011 and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each annual submission will conclude no earlier than 60 days before the submission date for that assessment. The iPLEDGE Program assessment will be submitted so that it is received by FDA on or before the due date.
The iPLEDGE Program

The Guide to Best Practices For The iPLEDGE Program

The resource to help the prescriber prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment

WARNING
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. In addition, for female patients of reproductive potential, isotretinoin is indicated only for those female patients who are not pregnant (see boxed CONTRAINDICATIONS AND WARNINGS and PRECAUTIONS sections).

IMPORTANT FACTS ABOUT ISOTRETINOIN

- Isotretinoin is highly teratogenic.
- Treatment with isotretinoin during pregnancy is contraindicated. Female patients should not be pregnant or become pregnant while on isotretinoin therapy and for 1 month thereafter.
- Fetal exposure to isotretinoin may result in life-threatening congenital abnormalities.

THE GUIDE TO BEST PRACTICES FOR THE iPLEDGE® PROGRAM

This guide has been developed to assist you in fulfilling the requirements for isotretinoin pregnancy prevention risk management. Please refer to the CONTRAINDICATIONS AND WARNINGS and the PRECAUTIONS sections of the isotretinoin Package Insert.

CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate.

Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately, and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

SPECIAL PRESCRIBING REQUIREMENTS

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE®. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program (see PRECAUTIONS).
TABLE OF CONTENTS

About isotretinoin ................................................................. 6
The iPLEDGE Program .......................................................... 8
Key information for prescribers .............................................. 10
iPLEDGE Program prescribing checklists ................................ 11
The iPLEDGE web site and phone system ............................. 13
Program materials ................................................................. 14
Activating registration .......................................................... 17
Delegates and office staff ...................................................... 18
Activating designee registration ............................................ 20
Overview: program requirements ........................................... 21
Determine reproductive potential of female patients .............. 27
iPLEDGE Program prescribing information ............................ 35
In the event of pregnancy ...................................................... 38
**About Isotretinoin**

Isotretinoin is used to treat severe recalcitrant nodular acne. Isotretinoin belongs to a class of drugs known as retinoids, commonly understood to include all natural and synthetic analogues of vitamin A. Treatment with isotretinoin should not be undertaken before conventional treatment has been tried first, including the use of systemic antibiotic therapy, and the patient has been fully counseled about the warnings and precautions in the isotretinoin package insert.

**Isotretinoin is teratogenic** and must not be used by pregnant women. Women should not become pregnant while taking isotretinoin or for 1 month after treatment is discontinued. A patient who becomes pregnant during treatment should stop taking isotretinoin and immediately contact her prescriber.

Isotretinoin use is associated with other potentially serious adverse events as well as more frequent, but less serious side effects. More frequent, less serious side effects include cheilitis, dry skin, skin fragility, pruritus, epistaxis, dry nose and dry mouth, and conjunctivitis.

Serious Adverse Event Warnings include psychiatric disorders* (depression, psychosis, and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors). Prescribers should read the brochure *Recognizing Psychiatric Disorders in Adolescents and Young Adults: A Guide for Prescribers of Isotretinoin*. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin treatment, patients and family members should be asked about any history of psychiatric disorder, and at each visit during treatment patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary.

Other Serious Adverse Events include pseudotumor cerebri; pancreatitis; hyperlipidemia; hearing impairment*; hepatotoxicity; inflammatory bowel disease; skeletal changes† (bone mineral density changes, hyperostosis, premature epiphyseal closure); and visual impairment (corneal opacities, decreased night vision).

Patients should be reminded to read the Medication Guide, distributed by the pharmacist at the time the isotretinoin is dispensed.

*No mechanism of action has been established for these events.
† The use of isotretinoin in patients 12 to 17 should be given careful consideration especially when a known metabolic or structural bone disease exists.
Pregnancy After Isotretinoin Treatment

The terminal elimination half-life of isotretinoin varies but is generally within 10 to 20 hours. The elimination half-life of 1 of the isotretinoin metabolites, 4-oxoisotretinoin, is approximately 25 hours. Since plasma elimination is host dependent, prescribers should warn patients not to become pregnant for 1 month post treatment. Women who become pregnant during this month should be counseled as to the outcome data. In 1989, Dai et al reported the results of an epidemiologic study of pregnancies that occurred in women who conceived after discontinuing isotretinoin. They studied women from 5 days to more than 60 days between the last dose of isotretinoin and conception. The incidence of birth defects in former isotretinoin patients was not significantly different from the rate in the general population. Isotretinoin is found in the semen of male patients taking isotretinoin, but the amount delivered to a female partner would be about 1 million times lower than an oral dose of 40 mg. While the no-effect limit for isotretinoin-induced embryopathy is unknown, 20 years of postmarketing reports include 4 with isolated defects compatible with features of retinoid-exposed fetuses; however, 2 of these reports were incomplete, and 2 had other possible explanations for the defects observed.

Birth Defects

There is an extremely high risk that a deformed infant will result if pregnancy occurs while female patients are taking isotretinoin in any amount even for short periods of time. Potentially, any fetus exposed during pregnancy can be affected. Not every fetus exposed to isotretinoin has resulted in a deformed child. However, there are no accurate means of determining which fetus has been affected and which fetus has not been affected.

When isotretinoin is taken during pregnancy, it has been associated with fetal malformations, and there is an increased risk for spontaneous abortions and premature birth. The following human fetal abnormalities have been documented.

External Abnormalities

Skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate.

Internal Abnormalities

CNS abnormalities including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit; cardiovascular abnormalities; thymus gland abnormalities; parathyroid hormone deficiencies. In some cases death has occurred with certain of the abnormalities noted.

Reference ID: 4252185
The iPLEDGE® Program

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called the iPLEDGE Program.

The iPLEDGE Program is a computer-based risk management system that uses verifiable, traceable links between prescriber, patient, pharmacy, and wholesaler to control prescribing, using, dispensing, and distribution of isotretinoin.

The iPLEDGE Program is a single, shared (includes multiple manufacturers) Risk Evaluation and Mitigation Strategy (REMS) program with requirements for prescribers, pharmacies, patients, and wholesalers. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to:
- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program.

The Traceable Links of The iPLEDGE Program

Reference ID: 4252185

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Key Features of The iPLEDGE Program

The iPLEDGE Program has specific requirements for prescribers, patients, pharmacies, and wholesalers.

- The iPLEDGE Program system tracks and verifies critical program elements that control access to isotretinoin.
- Only prescribers registered with and activated in the iPLEDGE Program can prescribe isotretinoin.
- Prescribers or their office designee must enter required information (pregnancy test results, 2 methods of contraception used, confirmation of patient counseling) in the iPLEDGE Program system for patients to be qualified to receive a prescription after the patient correctly answers a few comprehension questions.
- Prescribers must document that all patients—and specifically females of reproductive potential—meet the requirements in the iPLEDGE Program.
- Only patients who are registered by prescribers in the iPLEDGE Program can receive isotretinoin.
- Females of reproductive potential must enter required information (2 methods of contraception used, answer questions on program requirements) in the iPLEDGE Program system in order to be qualified to receive a prescription.
- Only pharmacies registered with and activated in the iPLEDGE Program can dispense isotretinoin.
- Pharmacists must receive authorization from the iPLEDGE Program system to fill and dispense every isotretinoin prescription.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE Program.
- Manufacturers will only ship isotretinoin to iPLEDGE Program registered entities (e.g., direct vendor pharmacies, wholesalers).
- Wholesalers must register annually in the iPLEDGE Program. A registered wholesaler may distribute only FDA-approved isotretinoin product.
- Only wholesalers registered with the iPLEDGE Program can distribute isotretinoin.
- Registered wholesalers can only ship isotretinoin to wholesalers registered in the iPLEDGE Program with prior written consent from the manufacturer or pharmacies licensed in the US and registered and activated in the iPLEDGE Program.
Key Information For Prescribers

The key areas prescribers must understand and follow include:

- The Non-Compliance Action Policy (NCAP)
- The iPLEDGE® Program educational materials for prescribers and patients
- Activation in the iPLEDGE Program automated system
- Prescriber steps required “Before,” “During,” and “After” treatment with isotretinoin
- Specific program criteria and procedures for females of reproductive potential
- Education for all patients about isotretinoin and the iPLEDGE Program requirements
- Patient registration
- The initial and monthly procedures for prescribing isotretinoin and information on the requirements for pharmacists
- Information on what to do in the event of a pregnancy
- Prescriber delegates and office staff designees

Non-Compliance Action Policy (NCAP)

The Non-Compliance Action Policy was implemented to monitor compliance, address deviations, and institute appropriate corrective actions to improve minimization of drug exposure during pregnancy and compliance with elements to assure safe use under the iPLEDGE Program. The NCAP sets forth the principles by which Non-Compliance by iPLEDGE Program stakeholders will be evaluated. The NCAP can be found on the iPLEDGE Program web site at www.ipledgeprogram.com.
BEFORE TREATMENT

PLANNING
☐ Verify female patient qualification criteria (see page 27).
☐ Plan for office visits, counseling, pregnancy testing.
☐ Educate about isotretinoin and the contraception requirements of the iPLEDGE Program.
☐ Obtain the Patient Information/Informed Consent (for all patients) form.
☐ Screen with serum or urine pregnancy test, which may be performed in the prescriber’s office: must be negative for patient to enter the iPLEDGE Program system.
☐ Register patient in the iPLEDGE Program system and provide patient with an educational guide, which includes the Patient ID number on perforated, removable cards.

COUNSEL ON CONTRACEPTION
☐ Counsel patient in office or refer to healthcare professional with expertise in contraception. Please see “Referral for Contraception Counseling” section of this guide for information on referring for contraception counseling.
☐ Counsel patient that she must use 2 effective methods of contraception simultaneously for at least 1 month before starting treatment. There is a 30-day mandatory waiting period during which she must be using both chosen methods of birth control before she is eligible to begin treatment with isotretinoin.
☐ Obtain the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.
☐ Inform patient about confidential iPLEDGE Program Pregnancy Registry.

PRESCRIBE
☐ Order a pregnancy test using a CLIA-certified laboratory (at least 30 days after registration):
  • During the first 5 days of the menstrual cycle, OR
  • For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods of contraception for 1 month.
☐ Confirm patient counseling of program requirements in the iPLEDGE Program system.
☐ Enter pregnancy test results and the patient’s 2 methods of contraception in the iPLEDGE Program system within the 7-day prescription window, counting the date of specimen collection for the pregnancy test as DAY 1. Your patient will not be able to answer her comprehension questions and then obtain her prescription until you have completed this task.
☐ Provide a prescription for up to a maximum 30-day supply of isotretinoin.

DURING TREATMENT (at each monthly visit)
☐ Counsel patient on contraception adherence.
☐ Order a pregnancy test using a CLIA-certified laboratory.
☐ Confirm patient counseling of program requirements in the iPLEDGE Program system.
☐ Enter pregnancy test results and the patient’s 2 methods of contraception in the iPLEDGE Program system within the 7-day prescription window, counting the date of specimen collection for the pregnancy test as DAY 1. Your patient will not be able to answer her comprehension questions and then obtain her prescription until you have completed this task.
☐ Provide a prescription for up to a maximum 30-day supply of isotretinoin.

AFTER TREATMENT

AFTER THE LAST DOSE
☐ Order a pregnancy test using a CLIA-certified laboratory after the last dose.
☐ Enter pregnancy test results and the patient’s 2 methods of contraception in the iPLEDGE Program system.
  • If you do not enter the results of the pregnancy test at the conclusion of treatment, the patient will be classified as Lost to Follow-Up, and both you and the patient may be contacted for additional information.
☐ Counsel patient on contraception adherence for 30 more days.
☐ Counsel patient not to give blood for at least 1 month after the last dose.

ONE MONTH AFTER THE LAST DOSE
☐ Order a pregnancy test using a CLIA-certified laboratory.
☐ Enter pregnancy test results and the patient’s 2 methods of contraception in the iPLEDGE Program system.
  • If you do not enter the results of the pregnancy test at the conclusion of treatment, the patient will be classified as Lost to Follow-Up, and both you and the patient may be contacted for additional information.

Refer to page 38 for information about reporting pregnancies to the confidential iPLEDGE Program Pregnancy Registry.

Prescribing Checklist tear sheets are available from the iPLEDGE Program. To order see Additional Materials (page 14).
iPLEDGE® Program Checklist
Male Patients And Female Patients Who Cannot Get Pregnant

BEFORE TREATMENT

PLANNING
☐ Plan for monthly office visits.
☐ Educate patients about isotretinoin and the iPLEDGE Program.
☐ Obtain the Patient Information/Informed Consent (for all patients) form.
☐ Register patients in the iPLEDGE Program system and provide patient with an educational guide, which includes the Patient ID number on perforated, removable cards.

PRESCRIBE
☐ Confirm patient counseling of program requirements in the iPLEDGE Program system within the 30-day prescription window, counting the patient’s office visit as DAY 1. The patient will not be able to obtain his/her prescription until you have completed this task.
☐ Provide a prescription for up to a maximum 30-day supply of isotretinoin.

DURING TREATMENT
☐ Counsel patient on program adherence.
☐ Confirm patient counseling of program requirements in the iPLEDGE Program system within the 30-day prescription window, counting the patient’s office visit as DAY 1. The patient will not be able to obtain his/her prescription until you have completed this task.
☐ Provide a prescription for up to a maximum 30-day supply of isotretinoin.

AFTER TREATMENT

AFTER THE LAST DOSE
☐ Counsel patient not to give blood for at least 1 month after the last dose.

Prescribing Checklist tear sheets are available from the iPLEDGE Program. To order see Additional Materials (page 14).
The iPLEDGE Program Web Site And Phone System

The prescriber can access the iPLEDGE Program system via the program web site and automated phone system:

- Web site: [www.ipledgeprogram.com](http://www.ipledgeprogram.com)
- Phone system: 1-866-495-0654

The iPLEDGE Program web site and phone system are used to:

- Activate prescriber registration
- Register office staff designees, who are then eligible to complete their activation
- Register patients
- Confirm patient counseling monthly for all patients for each prescription
- Enter monthly pregnancy test results and contraception information for females of reproductive potential. The patient cannot answer her monthly questions until the prescriber has entered the pregnancy test results in the iPLEDGE Program system.
- Track the current status of a patient
- Order additional copies of iPLEDGE Program educational materials
- Manage delegates
- Find a participating pharmacy
- Enter and make changes to patient name, address, phone number, and date of birth
- Edit prescriber name, specialty, address, phone and fax numbers, e-mail address, and preferred method of communication (US mail or e-mail)

Logging in to either the web site or phone system requires a username and password, which are supplied upon registration.
**Program Materials**

The iPLEDGE® Program provides educational materials for prescribers, pharmacists, and patients.

**Prescriber Materials**

It is important that the prescriber reviews the materials in the educational kit.

1. *Guide to Best Practices For The iPLEDGE Program* describes the requirements of the iPLEDGE Program for prescribers and for male and female patients.

2. *Prescriber Contraception Counseling Guide* is an overview of the effective methods of contraception and is a companion to the patient *Birth Control Workbook*.

3. The brochure *Recognizing Psychiatric Disorders in Adolescents And Young Adults* contains important information about depression, suicide, and psychiatric assessment and referral of your patients.

**Additional Materials**

Additional resource materials can be viewed on the iPLEDGE Program web site. These include:

- Isotretinoin Medication Guide
- Isotretinoin Package Inserts
- Prescribing Checklists
- Isotretinoin Contraception Referral Form
- Prescriber Activation Instructions
- Instructions for Registering and Managing Office Staff Designees
- Patient and Prescriber Flowcharts
- FAQs (Frequently Asked Questions)
Patient Materials

The prescriber distributes the Patient Introductory Brochure to patients considering taking isotretinoin. A patient educational kit, which provides information about the iPLEDGE Program requirements, should be given to the patient when they are registered in the iPLEDGE Program.

All materials include:

- The appropriate patient guide—the Guide to Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant or the Guide to Isotretinoin For Female Patients Who Can Get Pregnant
- The Patient Information/Informed Consent (for all patients) form
- Safety Information About Isotretinoin
- The patient ID card and number

Additionally, the kit for females of reproductive potential includes:

- The Contraception Counseling Guide And Contraception Referral Form. This includes the form to refer your patient to a contraception expert for counseling and a guide for the counselor about the requirements of the iPLEDGE Program.
- The Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
- The Birth Control Information Sheet—a 1-page guide to iPLEDGE Program approved contraception
- The Birth Control Workbook. This provides in-depth information about effective methods of contraception with iPLEDGE and their optimal use.

Educational Video

Be Prepared, Be Protected and Be Aware: The Risk of Pregnancy While on Isotretinoin. These describe the kind of birth defects that may happen if a woman takes any amount of isotretinoin while she is pregnant and also review reasons for contraception failure.
Patient Materials (Cont.)

Additional Educational Materials

You can order additional program materials using either the web site or the phone system as follows:

1. After logging on to the web site, there are 2 ways to order materials:
   a. Using the navigation menu on the left side of the page, select the “Order Materials” button.
   OR
   b. Using the navigation menu on the left side of the page, choose “Prescriber Information.” In the “View Information Online” section, select “To Order Educational Materials, please click here.”

2. In the phone system, log in and select the option to “Request Program Information.”

Materials will be shipped via ground delivery, and should arrive in 5 to 7 business days. The prescriber address in the iPLEDGE® Program at the time of the order will be used for the shipping destination. This address can be changed by the user as needed to direct shipments to specific desired locations.
Activating Registration

iPLEDGE registration must be activated in the iPLEDGE Program system before a prescriber can prescribe isotretinoin. Activation must occur annually.

The iPLEDGE Program system will report the expiration date of the prescriber’s activation. To retrieve this information, the prescriber:

- On the web site, logs in and chooses “My Program Status” on the left navigation
- In the phone system, logs in and selects the option to hear “Program Status”

The prescriber should review the *Guide To Best Practices for the iPLEDGE Program* and the *Prescriber Contraception Counseling Guide* to understand the program requirements. Activation requires the prescriber to attest to the following statements in the iPLEDGE Program system:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I know the risk factors for unplanned pregnancy and the effective measures for avoidance of unplanned pregnancy.
- I have the expertise to provide the patient with detailed pregnancy prevention counseling or I will refer her to an expert for such counseling, reimbursed by the manufacturer.
- I will comply with the iPLEDGE Program requirements described in the booklets entitled *Guide To Best Practices for the iPLEDGE Program* and *Prescriber Contraception Counseling Guide*.
- Before beginning treatment of females of reproductive potential with isotretinoin, and on a monthly basis, the patient will be counseled to avoid pregnancy by using 2 methods of contraception simultaneously and continuously for at least one month prior to initiation of isotretinoin treatment, during isotretinoin treatment and for one month after discontinuing isotretinoin treatment, unless the patient commits to continuous abstinence.
- I will not prescribe isotretinoin to any female of reproductive potential until verifying she has a negative screening pregnancy test and monthly negative CLIA-certified (Clinical Laboratory Improvement Amendment) pregnancy tests. Patients should have a pregnancy test at the completion of the entire course of isotretinoin and another pregnancy test one month later.
- I will report any pregnancy case that I become aware of while the female patient is on isotretinoin or one month after the last dose to the pregnancy registry.
Procedures For Activating in The iPLEDGE® Program System

The prescriber can access the iPLEDGE Program system to activate registration via the web site, www.ipledgeprogram.com, or the automated phone system, 1-866-495-0654. The web site is the faster and easier way to access the system. Identification in either system requires the username (DEA number or program-generated username) and password received with the registration materials. For information on the internet browsers compatible with the iPLEDGE Program web system, consult the FAQs on the home page of the site, www.ipledgeprogram.com.

The system requires setting the prescriber’s Date of Personal Significance. This is a date that the prescriber will be able to easily remember. It will be used to verify prescriber identity if needed by the iPLEDGE Program system or if a password is lost.

After initial activation, a prescriber must re-activate at least annually to remain active in the iPLEDGE Program. The iPLEDGE Program system will display the “Activate” button on the Prescriber home page when the activation for a prescriber is nearing expiration. However, a prescriber can re-activate at any time using the “Prescriber Activation” button on the left-hand navigation menu on all pages.

Delegates And Office Staff

The iPLEDGE Program allows the prescriber to delegate patient management to other prescribers registered with the iPLEDGE Program (these are known as delegates) and to designate office staff to assist with data entry (these are known as designees).

Delegating to Another Prescriber

The prescriber can manage delegates by going to the prescriber home page at www.ipledgeprogram.com. The prescriber must first add the name and required information for delegates into the iPLEDGE Program system. This function also allows the prescriber to define time frames for delegation and add or delete delegates.

Office Designees

The iPLEDGE Program provides a unique username and password to identified office staff to allow them to perform the following activities for the prescriber:

- Register patients and maintain the patient’s information in the iPLEDGE Program
- Enter patient pregnancy results
- Confirm patient counseling
- Discontinue patients
- Manage delegates
- Check patient’s program status
The following functions are available only to a prescriber:

- Prescriber registration
- Prescriber activation—initial and renewal
- Serious Medical Reasons Exemption process

A prescriber may have 1 or more office staff designees. Designees may be associated with 1 or more prescribers.

- They need to register and upon their initial activation they can work with multiple prescribers who assign them as designees. However, the designee must attest and activate annually.
- They may support all the registered prescribers in a multiphysician practice.
- They have rights for any patient delegated to an assigned prescriber.

Rights to perform the functions depend on the prescriber’s rights and program status.

- If a prescriber is not activated in the iPLEDGE Program system, neither the prescriber nor the designated office staff can register a patient.

**Designated office staff may access the automated system but must provide their own user ID and Date of Personal Significance as identifiers. Designees should not access the iPLEDGE system using an ID other than their own under any circumstances.**

**Please note:** The registered and activated prescriber is responsible for all information entered and activities performed in the iPLEDGE Program system by the office staff designee.

**To Designate Office Staff**

The prescriber:

1. Logs in to the web site, [www.ipledgeprogram.com](http://www.ipledgeprogram.com)
2. Chooses “Manage Delegates/Designees” from the Prescriber home page
3. Chooses “Register New Designee” from the Manage Delegates and Designees page
4. Fills in the required information on the registration online form
5. Selects “Save and Print” to save the new information and print the registration form

The office staff designee:

1. Signs and dates the completed form
2. Faxes or mails the completed form to the number or address provided

A username and password will be mailed to the designee upon completion of the registration process. The designee uses them:

- To log in to the automated system
- On the first log-in, to reset password and choose a Date of Personal Significance as a system identifier and to attest to the iPLEDGE Program requirements
Activating Designee Registration

iPLEDGE® Program registration must be activated in the iPLEDGE Program system before a designee can interact with the iPLEDGE Program.

The designee should review the Guide to Best Practices For The iPLEDGE Program and the Prescriber Contraception Counseling Guide to understand the program. Activation requires the designee to acknowledge the following statements in the iPLEDGE Program system annually:

- **Isotretinoin is teratogenic and must not be used by pregnant women.** The goals of the iPLEDGE Program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin’s serious risks and safe-use conditions. With these program goals in mind, iPLEDGE data are routinely analyzed to identify actions of Non-Compliance.

- **Information entered into the iPLEDGE Program system is considered part of the patient’s medical record, and can be used to investigate suspected Non-Compliance.** Verified Non-Compliance with regard to the iPLEDGE Program requirements can result in Permanent Deactivation from the iPLEDGE Program.

- **Prescribers are responsible for all iPLEDGE Program activities performed by their office staff designees.** If an office staff designee is found to be non-compliant with the iPLEDGE Program, resulting actions, including possible Permanent Deactivation from the iPLEDGE Program, can include both the designee and the prescriber.

- **Verified Non-Compliance may be reported to the FDA.**

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
Overview: Program Requirements

The iPLEDGE Program has specific requirements for prescribers, patients, and pharmacists. One of the prescriber's main responsibilities is knowing and educating patients about these requirements.

Prescribers are responsible for registering every patient who meets the program requirements in the iPLEDGE Program via the automated system. They are responsible for educating patients about the side effects of isotretinoin and the high risk of birth defects for females of reproductive potential while taking the drug. As part of this process, they are also responsible for counseling patients about the monthly steps they must follow to receive isotretinoin.

Prescribers can only write a patient's prescription for isotretinoin for up to a maximum of a 30-day supply. Patients must plan for monthly appointments to receive their prescriptions. At each of these appointments, the prescriber must counsel the patient about the iPLEDGE Program requirements and then confirm via the iPLEDGE automated system that this counseling occurred.

| All patients have a specific period of time in which they can obtain their prescription. This is called the “prescription window” and its start and end dates depend on the type of patient, as follows: |
|---|---|
| **Female patients who can get pregnant** | **Male patients and female patients who cannot get pregnant** |
| The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1. To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken. | The prescription window is 30 days, and starts on the date the prescriber enters as the date of the office visit. This date is counted as DAY 1. To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit. |

*After 11:59 p.m. Eastern Time on the last day of the prescription window, the prescription can no longer be picked up, and the patient must start the process over to get a new prescription window.*

*One notable exception is that females of reproductive potential who do not obtain their first month of treatment prescription in their first 7-day prescription window, must wait at least 19 days from their most recent pregnancy test until getting their new pregnancy test. This is based on the requirement that the most recent pregnancy test prior to beginning treatment must be conducted in the first 5 days of her menstrual cycle.

There are different program requirements for male patients and females of non-reproductive potential and for females of reproductive potential.
Overview: Program Requirements (Cont.)

All patients have a specific period of time in which they can obtain their prescription. This is called the “prescription window” and its start and end dates depend on the type of patient, as follows:

Female Patients Who Can Get Pregnant

The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1. To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken.

The prescriber must determine if a patient is a female of reproductive potential (see page 27) and document that she meets the specific requirements of the program. The requirements include the patient taking pregnancy tests and using 2 methods of birth control consistently for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment. To receive monthly prescriptions, a female of reproductive potential must also answer questions in the iPLEDGE® Program system about the program requirements and pregnancy prevention. Answering these questions can only take place after the prescriber has confirmed counseling and entered the pregnancy test result and the patient’s 2 methods of contraception (or committing to abstinence) into the system. In addition to answering the questions, the patient must also enter the 2 methods of birth control she is using (or indicate that she is relying on abstinence).

The pregnancy test can be obtained prior to, at the time of, or after the office visit. However, the 7-day prescription window will begin with the date that the specimen draw was performed.

Male Patients and Female Patients Who Cannot Get Pregnant

The prescription window is 30 days, and starts on the date the prescriber enters as the date of the office visit. This date is counted as DAY 1. To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit.

There are different program requirements for male patients and females of non-reproductive potential and for females of reproductive potential.

These are the criteria the system uses to authorize a pharmacy to fill and dispense a prescription.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Requirements For All Patients

To receive isotretinoin, all patients must meet all of the following conditions:

1. **Must** be registered with the iPLEDGE Program by the prescriber

2. **Must** understand that severe birth defects can occur with the use of isotretinoin by female patients

3. **Must** be reliable in understanding and carrying out instructions

4. **Must** sign a Patient Information/Informed Consent (for all patients) form that contains warnings about the potential risks associated with isotretinoin

5. **Must** obtain the prescription within their prescription window as follows:
   - Male patients and female patients who cannot get pregnant must obtain their prescription within the 30-day prescription window, counting the office visit as DAY 1.
   - Female patients who can get pregnant must obtain their prescription within 7 days of their pregnancy test, which is determined by the date of the blood draw or urine sample used in the test. The pregnancy test can be obtained before, during, or after the office visit.

6. **Must** not donate blood while on isotretinoin and for 1 month after treatment has ended

7. **Must** not share isotretinoin with anyone, even someone who has similar symptoms

All patients should understand that refills are not allowed. Patients can only receive a maximum of 30-day supply of isotretinoin per prescription. For each prescription, continuation of treatment requires the patient to satisfy the iPLEDGE Program requirements to obtain a new prescription. The prescriber must also counsel the patient each month about the iPLEDGE Program requirements and then confirm via the iPLEDGE Program automated system that this counseling occurred.
Requirements For All Patients (Cont.)

Females of Reproductive Potential Must:

- Be counseled on isotretinoin, the iPLEDGE® Program, and contraception requirements
- Sign the Patient Information/Informed Consent (for all patients) form
- Have an initial pregnancy test, which may be performed in the prescriber’s office
- Be registered in the iPLEDGE Program
- Use 2 methods of contraception together for sexual intercourse for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment
- Sign the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
- There is a 30-day mandatory waiting period during which females of reproductive potential must be using both chosen methods of birth control simultaneously before they are eligible to begin treatment with isotretinoin.
- Have a second pregnancy test within the first 5 days of the menstrual cycle, performed in a CLIA-certified laboratory, after being on 2 iPLEDGE Program approved methods of contraception for 1 month before starting isotretinoin treatment.* This second pregnancy test must be at least 19 days after the initial pregnancy test.
- Fulfill monthly requirements before receiving each prescription:
  - Have a serum or urine pregnancy test performed in a CLIA-certified laboratory
  - Access the system to answer questions about the iPLEDGE Program requirements and pregnancy prevention
  - Enter into the iPLEDGE Program system the 2 methods of contraception being used
- Have a pregnancy test after their last dose, performed in a CLIA-certified laboratory
- Continue using 2 methods of contraception for 1 month after their last dose
- Have a pregnancy test 1 month after their last dose

*For timing information about monthly pregnancy tests, see “Requirements for Females of Reproductive Potential” on page 28.
About The Patient Questions

Prior to being able to obtain a prescription, females of reproductive potential must answer questions about the iPLEDGE Program and pregnancy prevention. These questions must be answered after their prescriber has confirmed counseling, entered pregnancy test results and 2 contraceptive methods (or commitment to abstinence) into the iPLEDGE Program system, but before the 7-day prescription window for their prescription expires. Patients answer these questions via the web site or phone system. (Access information is provided in the patient guide.) The patient may use her patient guide and the Birth Control Workbook to help with the answers.

The system provides questions in several specific categories and correct answers for those questions, with references to the appropriate patient education material. A replacement question in the same category is provided for an incorrectly answered question.

If a patient misses a replacement question, the iPLEDGE Program system will direct her to review her materials and try again at a later time. She may also contact her prescriber so that her program education and counseling can be reinforced. The patient should also review her educational materials and then answer the questions again.

Requirements For Pharmacists

- Isotretinoin can only be obtained from pharmacies registered with and activated in the iPLEDGE Program.
- Registered and activated pharmacies can obtain isotretinoin only from wholesalers registered with the iPLEDGE Program.
- The dispensing pharmacist must receive authorization from the iPLEDGE Program system to fill and dispense every isotretinoin prescription.
- Upon receiving authorization, the dispensing pharmacist can fill and dispense a prescription for a maximum 30-day supply of isotretinoin.
- Upon authorization, the iPLEDGE Program system provides a “Do Not Dispense To Patient After” date. This date is calculated as 30 days from the office visit for male patients and females of non-reproductive potential, or 7 days from the pregnancy test date for females of reproductive potential. It is recommended that the pharmacy staff record this date on the prescription bag sticker.
- Prescriptions that are more than 30 days beyond the date of the office visit (for male patients and females of non-reproductive potential) or more than 7 days beyond the pregnancy test date (for females of reproductive potential), will not be authorized by the iPLEDGE Program system.
Requirements For Pharmacists (Cont.)

- Prescriptions must be obtained no later than the “Do Not Dispense To Patient After” date, and if not obtained, then the Risk Management Authorization (RMA) must be reversed in the iPLEDGE® Program system and the product returned to inventory.
  - No automatic refills are permitted.
  - Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.
  - An isotretinoin Medication Guide must be given to the patient each time isotretinoin is dispensed, as required by law.

Pharmacy Information

Patients can only obtain isotretinoin prescriptions from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

The web site, www.ipledgeprogram.com, provides a database of registered pharmacies. Patients and prescribers can access this information by logging in and choosing the “Find a Participating Pharmacy” button on their home page.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found on the iPLEDGE Program web site www.ipledgeprogram.com or by calling 1-866-495-0654.

NOTE: The iPLEDGE Program Sponsors monitor and investigate Patient classification, and you may be required to provide documentation to support your Patient classification request. Intentional falsification of Patient classification type that is determined to be an attempt to violate program requirements is defined as non-compliance in the Non-Compliance Action Policy. This may result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privilege.
Determine Reproductive Potential of Female Patients

Qualification Criteria

The prescriber must determine if a female is of reproductive potential before enrolling her in the iPLEDGE Program. The definition of a female of reproductive potential is a female who has not had a hysterectomy, bilateral oophorectomy, or is not post-menopausal. This definition includes a young woman who has not yet started menstruating.

- A woman who has had a tubal sterilization is considered a female of reproductive potential in the iPLEDGE Program.

Definition of Menopause

Menopause can be assumed to have occurred in a woman when there is either:

1. Appropriate medical documentation of prior complete bilateral oophorectomy (i.e., surgical removal of the ovaries, resulting in “surgical menopause” and occurring at the age at which the procedure was performed), OR

2. Permanent cessation of previously occurring menses as a result of ovarian failure with documentation of hormonal deficiency by a certified healthcare provider (i.e., “spontaneous menopause,” which occurs in the United States at a mean age of 51.5 years).

Hormonal deficiency should be properly documented in the case of suspected spontaneous menopause as follows:

1. If age >54 years and with the absence of normal menses: Serum FSH (Follicle Stimulating Hormone) level elevated to within the post-menopausal range based on the laboratory reference range where the hormonal assay is performed;

2. If age <54 years and with the absence of normal menses: Negative serum or urine -HCG with concurrently elevated serum FSH (Follicle Stimulating Hormone) level in the post-menopausal range, depressed estradiol (E2) level in the post-menopausal range, and absent serum progesterone level, based on the laboratory reference ranges where the hormonal assays are performed.
Female Patient Qualification Criteria (Cont.)

Screen Patients

Data support that there are key issues in identifying female patients for treatment with isotretinoin.

The prescriber should:

1. Identify patients whose acne could be effectively managed without isotretinoin and avoid prescribing it for such patients
2. Identify those who are already pregnant when considering isotretinoin
3. Identify those who may not be reliable in avoiding pregnancy for the required period before, during, and after treatment

The patient should understand that, ultimately, it is her responsibility to avoid exposing an unborn baby to isotretinoin. The patient must understand the critical responsibility she assumes in electing to undertake treatment with isotretinoin and that any method of birth control, apart from complete abstinence, can fail.

The prescriber must verify that each individual patient receives adequate counseling about all her pregnancy prevention options (including abstinence) and that she knows how to select and use 2 separate, effective contraceptive methods.

Requirements For Females of Reproductive Potential

Once the prescriber decides to pursue qualification of the patient, a female of reproductive potential must follow these steps.

1. Before the patient can begin isotretinoin treatment, there is a 30-day wait period where the patient must be on 2 methods of birth control simultaneously. Additionally, she will need to have 2 negative pregnancy tests. Females of reproductive potential must have had 2 negative urine or serum pregnancy tests with a sensitivity of at least 25 mIU/mL before receiving the initial isotretinoin prescription. The first test (a screening test) is obtained by the prescriber when the decision is made to pursue qualification of the patient for isotretinoin. The second pregnancy test (a confirmation test) must be done in a CLIA-certified laboratory. The interval between the 2 tests must be at least 19 days.

   • For patients with regular menstrual cycles, the second pregnancy test must be done during the first 5 days of the menstrual period immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods of contraception for 1 month.

   • For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods of contraception for 1 month.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
• The patient must be using her 2 methods of contraception for at least 30 days prior to beginning treatment on isotretinoin, and her second pregnancy test must occur after this 30-day period is complete.

2. The patient must sign the Patient Information/Informed Consent (for all patients) form and the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.

3. The patient must select and commit to use 2 methods of effective contraception simultaneously, at least 1 of which must be a primary method, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Patients must use 2 methods of effective contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment. Counseling about contraception and behaviors associated with an increased risk of pregnancy must be repeated on a monthly basis prior to issuing each prescription.

Monthly Requirements During Treatment

Each month of treatment, patients must have a negative result from a urine or serum pregnancy test. A pregnancy test must be repeated each month, in a CLIA-certified laboratory, prior to the female patient receiving each prescription. The iPLEDGE® Program also requires monthly counseling about contraception and behaviors associated with an increased risk of pregnancy. In addition to their required doctor/prescriber appointments, females of reproductive potential each month must also enter their 2 effective methods of contraception in the iPLEDGE Program system and answer questions about the iPLEDGE Program and pregnancy prevention.

Requirements at The End of Treatment

A pregnancy test must also be ordered at the end of treatment (after the last dose). If the results of the pregnancy tests at the conclusion of treatment, are not entered into the iPLEDGE Program system, the patient will be classified as Lost to Follow-Up, and both the prescriber and the patient will be contacted for additional information.

Requirements 1 Month After Discontinuing Treatment

A pregnancy test must also be ordered 1 month after the last dose. If the results of the pregnancy tests 1 month after the conclusion of treatment, are not entered into the iPLEDGE Program system, the patient will be classified as Lost to Follow-Up, and both the prescriber and the patient will be contacted for additional information.
<table>
<thead>
<tr>
<th>Primary Method of Birth Control (Choose One)*</th>
<th>How to Use it</th>
<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks†</th>
</tr>
</thead>
</table>
| Hormonal Implant                              | Placed under skin of arm by a clinician. Works for 3 years.¹ | >99%¹ | • Nothing to do or remember  
• Light or no periods  
• May decrease acne  
• No increased risk of clots | • Irregular Periods |
| Hormonal IUD                                  | Placed in uterus by clinician. Self-check monthly. Works for 5 years.³ | >99%³ | • Light or no periods  
• No increased risk of clots | • Irregular Periods |
| Non-Hormonal IUD                              | Placed in uterus by a clinician. Self-check monthly. Works for 10 years.⁴ | >99%⁴ | • No hormones  
• Periods remain regular  
• Effective immediately  
• No increased risk of clots | • May cause heavier periods and cramping |
| Tubal Sterilization                           | Surgical procedure to close the tubes between the uterus and the ovaries. | >99%⁵ | • It is a virtually permanent method of birth control  
• Nothing to do or remember | • If you want to have child later, it is very difficult to re-open the tubes |
| Male Vasectomy                                | Surgical procedure that closes off the tubes that carry a partner’s sperm. | >99%⁵ | • It is a virtually permanent method of birth control  
• Nothing to do or remember | • If you want to have child later, it is very difficult to re-open the tubes |
| Hormonal Shot                                 | Given every 3 months by a clinician. | >97%¹ | • Light or no periods  
• No increased risk of clots | • Irregular Periods  
• May cause weight gain |
| Vaginal Ring                                  | You place in vagina. Replace monthly. | 92%¹ | • Lighter periods  
• May decrease acne | • Blood clots |
| Hormonal Patch                                | You place on skin. Replace weekly. | 92%¹ | • Lighter periods  
• May decrease acne | • Blood clots |
| Birth Control Pill (Combination Type)         | Swallow at the same time daily. | 92%¹ | • Lighter periods  
• May decrease acne | • Blood clots |

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.
†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Reference ID: 4252185
Table 1: Primary Methods of Contraception by Typical Use Failure Rate

<table>
<thead>
<tr>
<th>Method</th>
<th>Typical Use Failure Rate</th>
<th>Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantable Hormones</td>
<td>0.05%</td>
<td>0.05%</td>
</tr>
<tr>
<td>Male Vasectomy</td>
<td>0.10%</td>
<td>0.15%</td>
</tr>
<tr>
<td>Hormonal IUD (LNg 20)</td>
<td>0.20%</td>
<td>0.20%</td>
</tr>
<tr>
<td>Tubal Sterilization</td>
<td>0.50%</td>
<td>0.50%</td>
</tr>
<tr>
<td>Non-hormonal IUD (Copper T380A)</td>
<td>0.60%</td>
<td>0.80%</td>
</tr>
<tr>
<td>Hormonal Injectable (single)</td>
<td>0.20%</td>
<td>6.00%</td>
</tr>
<tr>
<td>Hormonal Transdermal Patch</td>
<td>0.30%</td>
<td>9.00%</td>
</tr>
<tr>
<td>Hormonal Vaginal Ring</td>
<td>0.30%</td>
<td>9.00%</td>
</tr>
<tr>
<td>Hormonal Combination Oral Contraceptives</td>
<td>0.30%</td>
<td>9.00%</td>
</tr>
</tbody>
</table>


b. The IUD Progesterone T and progestin-only “mini-pills” are not acceptable for the iPLEDGE® Program. (See “Unacceptable Methods Of Contraception” on page 32).

Table 2: Secondary Methods of Contraception Listed by Typical Use Failure

<table>
<thead>
<tr>
<th>Method</th>
<th>Typical Use Failure Rate</th>
<th>Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrier Methods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Latex Condomb</td>
<td>2%</td>
<td>18%</td>
</tr>
<tr>
<td>Diaphragm*</td>
<td>6%</td>
<td>12%</td>
</tr>
<tr>
<td>Cervical Cap*</td>
<td>9%</td>
<td>20%</td>
</tr>
<tr>
<td>Other Methods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal Spongec</td>
<td>9%</td>
<td>12%</td>
</tr>
</tbody>
</table>

b. Male latex condom failure rates are for use without spermicide. Female condoms are not acceptable for the iPLEDGE® Program. (See “Unacceptable Methods Of Contraception” on page 32.)
c. Failure rate for nulliparous women. The rate is approximately double for parous women.

*Failure rates for diaphragm and cervical cap are for methods including the use of spermicide.
Unacceptable Methods of Contraception Include:

- Progesterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method or fertility awareness)
- Breastfeeding
- Withdrawal
- Cervical shield*

Abstinence

For this program, all females of reproductive potential must fully commit to pregnancy prevention. Isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE® Program. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence, she must understand that she has committed to not engaging in sexual activity for 1 month before she starts taking isotretinoin, while she is on isotretinoin and for 1 month after she stops taking isotretinoin.

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.

Contraception Counseling

The prescriber must ensure that each individual patient receives adequate counseling about all her pregnancy prevention options (including abstinence) and that she knows how to select and use 2 separate, iPLEDGE Program–effective methods of contraception that will give her the lowest failure rate.

The patient must understand the critical responsibility she assumes in electing to undertake treatment with isotretinoin and that any method of birth control, apart from complete abstinence, can fail. All females of reproductive potential must read the patient Birth Control Workbook.

*A cervical shield should not be confused with a cervical cap, which is an effective secondary method of contraception.
Reinforce The Importance of Using 2 Effective Methods of Birth Control

In the US, the pregnancy rate for females between the ages of 15-44 who were trying not to get pregnant was 51/1000 and 48% of those females were using birth control in the month they got pregnant.\(^2\)

When counseling patients on contraception, the prescriber should refer to the \textit{Prescriber Contraception Counseling Guide}, which contains an overview of issues in contraception and the effective methods of contraception in the iPLEDGE Program. It is a companion to the patient \textit{Birth Control Workbook}.

It is especially important to assess the patient’s ability to understand her contraception responsibilities and instructions provided by the prescriber. It is very important to be able to make a careful assessment of a female patient’s reproductive history, contraceptive knowledge, and previous use of contraception methods. This assessment and contraceptive education should continue throughout isotretinoin treatment.

Referral For Contraception Counseling

Before beginning treatment, the prescriber or patient may choose referral to a healthcare professional with expertise in pregnancy prevention. The makers of isotretinoin will reimburse 1 visit for contraception counseling. The patient educational kit contains the \textit{Contraception Counseling Guide and Contraception Referral Form}. The form is in the guide that outlines the contraception requirements and the approved methods of contraception in the iPLEDGE Program for the birth control expert.

The referral form should be taken to the contraception counselor by the patient or sent in advance. The form instructs the counselor to fill in the appropriate information and return it to the prescriber with the patient's contraception choices to enter into the iPLEDGE Program system. The reverse side of the form has information for the counselor on the reimbursement process.

Referring to a Gynecologist

The prescriber may want to specifically refer a patient to a gynecologist for:

- An examination prior to starting oral contraceptive agents or a hormonal transdermal patch
- Insertion of an IUD or hormonal vaginal ring
- Fitting a diaphragm or a cervical cap
- More detailed explanation of contraception options

Reference ID: 4252185
Referring to a Gynecologist (Cont.)

The prescriber may wish to ask for gynecologic consultation under the following circumstances:

- The patient’s history is suggestive of polycystic ovary syndrome (Stein–Leventhal syndrome). In addition to acne she may have:
  - Excessive facial hair growth (common when acne is present)
  - Obesity
  - Amenorrhea (no menstrual period) or irregular, heavy bleeding
  - Anovulation
- The patient has irregular menses, possibly related to pregnancy; an eating disorder; or endometriosis.
- There are indications of sexual abuse found during the physical examination or counseling session.
- There is history or are symptoms of sexually transmitted infection.
iPLEDGE® Program Prescribing Information

Register Patients in The iPLEDGE Program System

Patients may be registered in the iPLEDGE Program system either via the web site or phone system after obtaining the Patient Information/Informed Consent (for all patients) form and providing the patient with an ID number and ID card. The process is faster and easier using the web site.

On the web site, the prescriber logs in and chooses “Register New Patient.” In the phone system, the prescriber logs in and selects the option to “Register a New Patient.”

The system will request this specific patient information:

- Patient ID number
- Patient first and last name and middle initial
- Home address
- Phone number
- Date of birth
- Gender
- Last 4 digits of the Social Security number
- System-assisted classification of patient type (i.e., Female of reproductive potential, female of non-reproductive potential, or male)
- Screening pregnancy test date and results (for females of reproductive potential)

ID Number And ID Card

The ID number and perforated ID cards are provided with the patient education materials. It is important that patients do not lose the cards. Prescribers should keep a record of the patient's number.

- All patients need the ID number and ID card to obtain their prescriptions, and to access the web site or automated phone line.
- Females of reproductive potential will need their ID number to access the iPLEDGE Program system to answer questions about the iPLEDGE Program and preventing pregnancy.
iPLEDGE® Program Prescribing Information (Cont.)

Informed Consents

Patients will need to sign the following consent forms to be in the iPLEDGE Program.

- Patient Information/Informed Consent (for all patients)
- Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)

For females of reproductive potential, signing the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form means the following:

- They understand the teratogenic risks of isotretinoin.
- They agree to follow the contraception requirements of the iPLEDGE Program before, during, and for 1 month after their treatment with isotretinoin.

Prescriptions: iPLEDGE Program System Requirements

Before a patient can obtain a prescription for isotretinoin at a registered pharmacy, the iPLEDGE Program system requires that the information below be entered into the system and the timing criteria for filling and dispensing a prescription be met. This is the information that the system will use to authorize filling a prescription and to provide the “Do Not Dispense To Patient After” date.

All Patients

Prescriber confirms that:

- The patient is registered with the iPLEDGE Program.
- The patient was counseled on the iPLEDGE Program requirements.

Females of Reproductive Potential

Prior to the patient obtaining each prescription, the prescriber must access the iPLEDGE Program system to:

- Confirm that the patient was counseled about isotretinoin and the iPLEDGE Program contraception requirements
- Enter the 2 methods of contraception that the patient is using
- Enter pregnancy result into the iPLEDGE Program system, within the 7-day prescription window, counting the date of blood draw or urine sample as DAY 1
- The patient cannot answer her monthly questions and get a prescription filled until after these activities are completed by the prescriber.

A positive pregnancy test prevents the prescription from being filled.

Patient must access the iPLEDGE Program system after the prescriber has entered the pregnancy test results to:

- Correctly answer the questions about the iPLEDGE Program and pregnancy prevention
- Enter the 2 methods of contraception she is using

The primary method of contraception reported by both the prescriber and the patient must match.
Timing Criteria For The Prescription To Be Obtained From The Pharmacy

- All patients must obtain their prescriptions as follows:
  - For male and female patients who cannot get pregnant, prescriptions must be obtained within the 30-day prescription window, counting the office visit as DAY 1.
  - For female patients who can get pregnant, prescriptions must be obtained within the 7-day prescription window, counting the day of the blood draw or urine sample as DAY 1.
- Patients will not be able to obtain prescriptions after their prescription window has expired.

The iPLEDGE Program system will automatically provide the pharmacist with a “Do Not Dispense To Patient After” date, which is the end of the prescription window. The pharmacist cannot fill or dispense the patient’s prescription after that date.

After The Last Dose

All patients should be reminded not to give blood for at least 1 month after their last dose.

Females of Reproductive Potential Must Have Pregnancy Tests:

- After their last dose, and
- 1 month after their last dose
- If this information is not entered, the patient will be classified as Lost to Follow-Up, and both the prescriber and the patient will be contacted for more information.

It is important to stress the need for continued contraception during the 1 month after the last dose. Patients also should be reminded to enter their 2 methods of contraception.

Post-Treatment iPLEDGE Program Requirements

When a patient will no longer be taking isotretinoin, action is required by the prescriber to record specifics of the end of treatment. Specifically the following information is required by the iPLEDGE Program:

- If known when issuing the prescription, the prescriber will indicate that a prescription will be the last 1 for this patient. This will remind the prescriber of the patient requirements for post-treatment activity.
- The prescriber must discontinue the patient within the iPLEDGE Program.
- When discontinuing a patient through either the web site or the phone system, the prescriber must enter the Date of Last Dose, and the reason why this patient will no longer be taking isotretinoin. This reason will be selected from a list presented by the iPLEDGE Program system, including Completed Treatment, Pregnancy, or Other. On the web site, explanatory comments can also be provided, and may be required by the iPLEDGE Program system.
  - If the reason for discontinuation is related to an Adverse Event, please be as specific as possible in the comments entered in the iPLEDGE Program system.
Post-Treatment iPLEDGE® Program Requirements (Cont.)

- For females of reproductive potential, a final pregnancy test is required at the date of last dose, and 30 days after date of last dose.

If this information is not provided, and a patient has no activity in the iPLEDGE Program system for specific periods of time, the patient will be classified as Lost to Follow-Up. If this occurs, prescribers and patients will be contacted by the iPLEDGE Program.

In The Event of Pregnancy

Counseling a Pregnant Patient

If a pregnancy does occur during isotretinoin treatment, isotretinoin must be discontinued immediately. The patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Reporting Pregnancy

The iPLEDGE Program Pregnancy Registry

The iPLEDGE Program Pregnancy Registry collects data on pregnancies that occur in female patients who become pregnant while taking isotretinoin or within 1 month of their last dose. Data from the registry are reported to the FDA and are used to assess the effectiveness of the iPLEDGE Program. The data are also used to evaluate further ways to reduce fetal exposure. Information gathered in the iPLEDGE Program Pregnancy Registry will be used for statistical purposes only and will be held in the strictest confidence.

The prescriber must report to the iPLEDGE Program Pregnancy Registry any pregnancy case that he/she becomes aware of while the female patient is on isotretinoin or 1 month after the last dose. Report a pregnancy by calling 1-866-495-0654. Select the option to “Report a Pregnancy.” All pregnancies should also be reported to the FDA via the MedWatch number: 1-800-FDA-1088.
Reporting Pregnancy (Cont.)

In Female Patients Taking Isotretinoin

1. Positive pregnancy test results should be entered in the iPLEDGE Program system. A Safety Surveillance Associate will call the prescriber.

2. A prescriber should call the iPLEDGE Program Call Center if he or she does not have a pregnancy test result but thinks the patient is pregnant.

In Partners of Males Being Treated With Isotretinoin

If the prescriber becomes aware of a pregnancy in the partner of a male patient taking isotretinoin, the prescriber should report this pregnancy to the iPLEDGE Program Pregnancy Registry. The information will be forwarded to the manufacturer of the specific isotretinoin product for follow-up.

Males And Birth Defects

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin.

Studies did not show effects on sperm count, how sperm look, or how well they swim and move.

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.

References


For iPLEDGE Program Information

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
WARNING
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Prescriber Contraception Counseling Guide

The information prescribers should communicate to patients to help prevent pregnancies during the course of isotretinoin treatment
NOTES:

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
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________________________________________________________________________
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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>47</td>
</tr>
<tr>
<td>Counseling goals</td>
<td>48</td>
</tr>
<tr>
<td>Contraception requirements</td>
<td>49</td>
</tr>
<tr>
<td>Referring to a gynecologist</td>
<td>53</td>
</tr>
<tr>
<td>Obtaining a sexual and behavioral history</td>
<td>53</td>
</tr>
<tr>
<td>Contraception reference material</td>
<td>57</td>
</tr>
<tr>
<td>Primary methods of contraception</td>
<td>57</td>
</tr>
<tr>
<td>Secondary methods of contraception</td>
<td>71</td>
</tr>
<tr>
<td>Emergency contraception</td>
<td>76</td>
</tr>
<tr>
<td>Reporting a pregnancy</td>
<td>76</td>
</tr>
<tr>
<td>For more information about isotretinoin and the iPLEDGE® Program</td>
<td>79</td>
</tr>
</tbody>
</table>

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Introduction

This Prescriber Contraception Counseling Guide is intended to aid in counseling a female of reproductive potential who will be taking isotretinoin.

The patient must select and commit to using 2 methods of iPLEDGE Program approved contraception simultaneously, at least 1 of which must be a primary method, unless the patient commits to continuous abstinence (not engaging in sexual activity), or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Patients must use 2 methods of iPLEDGE Program approved contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment.

It is strongly recommended that a patient use a primary method of contraception and is committed to using a second method as well, even if she says she will be abstinent for the entire required period. Isotretinoin is not recommended for sexually active females of reproductive potential whom you believe will not be able to maintain abstinence or will not use contraception, as the program requires.

The contraceptive that a patient selects can have a dramatic effect on her chance of becoming pregnant. A patient needs to select methods that she and/or her partner will use correctly each time they have intercourse. This Prescriber Contraception Counseling Guide will help you enable the patient to select the 2 contraceptive methods that are consistent with the iPLEDGE Program guidelines and that she will use correctly and consistently.

Referral For Contraception Counseling

Before beginning treatment, the prescriber or patient may choose referral to a healthcare professional with expertise in pregnancy prevention. The makers of isotretinoin will reimburse 1 visit for contraception counseling. The Isotretinoin Educational Kit For Female Patients Who Can Get Pregnant contains the Contraception Counseling Guide And Contraception Referral Form. The referral form is in the guide, which outlines the contraception requirements and the effective methods of contraception of the iPLEDGE Program for the birth control expert.

Contraception counseling is an important part of the patient choosing her 2 contraceptive methods. If practitioners are not comfortable providing this counseling, they are encouraged to take advantage of the opportunity to refer patients to a qualified counselor.

The referral form should be taken to the contraception counselor by the patient or sent in advance. The form instructs the counselor to fill in the appropriate information and return it to the prescriber with the patient's contraception choices to enter into the iPLEDGE Program system. The reverse side of the form has information for the counselor on the reimbursement process.
Counseling About Contraception

Please read this *Prescriber Contraception Counseling Guide* completely before you begin your counseling session. The guide reviews the counseling goals and provides an overview of contraception choices from a pregnancy risk management context (necessary for females of reproductive potential taking isotretinoin), information on obtaining a sexual and behavioral history (including additional guidance for interviewing an adolescent), and contraception reference materials.

Patients in the iPLEDGE® Program receive the *Birth Control Workbook*, which contains information on effective primary and secondary methods of contraception. It is not complete information on any of the methods, and the patient is encouraged to ask questions about specific methods or issues.

Counseling Goals

**Ensure That The Patient:**

- Understands the risk of having a child with significant birth defects from exposure to isotretinoin.
- Understands the need for using 2 methods of contraception together consistently and correctly and knows when to contact her prescriber for emergency contraception (see page 76).
- Chooses the methods of contraception that will work best for her and that she and her partner will actually use. Adherence impacts the failure rate of hormonal combination oral contraceptives more strongly than other primary methods. (Please see “Hormonal Combination Oral Contraceptives as a Primary Method” on page 50.)
- Commits fully to not becoming pregnant and to using 2 methods of contraception simultaneously, consistently, and correctly. If, after counseling, the patient recognizes she will not be able to commit fully, encourage her to not take isotretinoin or do not prescribe.
- Is able and willing to maintain abstinence, if that is her choice after counseling. If a patient who has ever been sexually active chooses abstinence, and you believe that she will not be able to maintain abstinence and will not use contraception, encourage her to not take isotretinoin.
Counseling Younger Teens

For younger teens, it is important to stress the following aspects of contraception for the iPLEDGE Program during counseling:

- Effective primary and secondary birth control methods
- Why it is important to use two effective methods of birth control simultaneously, consistently, and correctly. Younger teens may need more emphasis on this point to fully understand it and comply.
- The role of emergency contraception. Younger teens may need specific direction from you to take immediate action if they had unprotected sex.

Contraception Requirements

Using 2 Methods of Contraception Provides More Protection

Use of two iPLEDGE Program approved methods of contraception (at least one of which is a primary method) simultaneously substantially reduces the risk that a female will become pregnant.

In the US, the pregnancy rate for females between the ages of 15-44 who were trying not to get pregnant was 51/1000 and 48% of those females were using birth control in the month they got pregnant.*

In addition, it is not known if hormonal contraceptives are less effective when used with isotretinoin.1 Because of this possibility and the fact that all contraceptive methods are less than 100% effective, the iPLEDGE Program requires the additional protection of a second method of contraception.

Selecting an Effective Primary Method of Contraception

Table 1 lists, by typical use failure rate, the primary methods of contraception acceptable in the iPLEDGE® Program. The single most important decision in contraception for the iPLEDGE Program is selecting a primary method that the patient can and will use as correctly as possible. Other important factors to consider in counseling the patient on selecting a primary method include side effects, contraindications, and the patient’s ability to use it correctly. All of these factors influence compliance with the iPLEDGE Program requirements to prevent pregnancy.

Table 1: Primary Methods of Contraception by Typical Use Failure Rate

<table>
<thead>
<tr>
<th>Method</th>
<th>Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Perfect Use</td>
</tr>
<tr>
<td>Implantable Hormones</td>
<td>0.05%</td>
</tr>
<tr>
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<td>0.10%</td>
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<td>Hormonal IUD (LNg 20)</td>
<td>0.20%</td>
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<td>Tubal Sterilization</td>
<td>0.50%</td>
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<tr>
<td>Non-hormonal IUD (Copper T380A)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.60%</td>
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<td>Hormonal Injectable (single)</td>
<td>0.20%</td>
</tr>
<tr>
<td>Hormonal Transdermal Patch</td>
<td>0.30%</td>
</tr>
<tr>
<td>Hormonal Vaginal Ring</td>
<td>0.30%</td>
</tr>
<tr>
<td>Hormonal Combination Oral Contraceptives&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.30%</td>
</tr>
</tbody>
</table>


b. The IUD Progesterone T and progestin-only “mini-pills” are not acceptable for the iPLEDGE® Program. (See “Unacceptable Methods Of Contraception” on page 52).

Hormonal Combination Oral Contraceptives as a Primary Method

If the patient is currently taking or planning to take oral contraceptives, review that section in the Birth Control Workbook with her.

For a patient who has indicated she has difficulty taking oral contraceptives correctly, other contraception not requiring daily dosing may be a better choice. It is critical that such a patient choose a method other than daily oral contraceptive agents.
Selecting an Effective Secondary Method of Contraception

Table 2 lists the acceptable secondary methods of contraception in the iPLEDGE Program. There are 2 methods of secondary contraception: barrier and other. Barrier methods include the diaphragm and cervical cap (both of which must be used with a spermicide) and the male latex condom (which can be used with or without a spermicide). The other method is the vaginal sponge, which contains a spermicide. The most important issue for a secondary method is that it be used correctly each time the patient has intercourse and that it be in place should the primary method fail.

Help the patient select a secondary method that she and/or her partner can fully commit to using correctly each time they have intercourse.

<table>
<thead>
<tr>
<th>Method</th>
<th>Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Usea</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td>Perfect Use</td>
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<tr>
<td>Barrier Methods</td>
<td></td>
</tr>
<tr>
<td>Male Latex Condomb</td>
<td>2%</td>
</tr>
<tr>
<td>Diaphragm*</td>
<td>6%</td>
</tr>
<tr>
<td>Cervical Cap*,a</td>
<td>9%</td>
</tr>
<tr>
<td>Other Methods</td>
<td></td>
</tr>
<tr>
<td>Vaginal Spongec</td>
<td>9%</td>
</tr>
</tbody>
</table>


b. Male latex condom failure rates are for use without spermicide. Female condoms are not acceptable for the iPLEDGE® Program (See “Unacceptable Methods Of Contraception” on page 52.)

c. Failure rate for nulliparous women. The rate is approximately double for parous women.

*Failure rates for diaphragm and cervical cap are for methods including the use of spermicide.
Unacceptable Methods of Contraception

The following methods of contraception are not acceptable for the iPLEDGE* Program:

- Progestosterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method or fertility awareness)
- Breastfeeding
- Withdrawal
- Cervical shield*

Patients currently using these unacceptable methods of contraception must switch to iPLEDGE Program approved methods of contraception.

Emergency Contraception

Review this section in the Birth Control Workbook with the patient. She should know when to call her prescriber for possible emergency contraception. She should also realize that emergency contraception should not be used on a regular basis as a replacement for the other contraceptive methods she selected.

Abstinence

For this program, all females of reproductive potential must fully commit to pregnancy prevention.

Isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE Program. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence, she must understand that she has committed to not engaging in sexual activity for 1 month before she starts taking isotretinoin, while she is on isotretinoin and for 1 month after she stops taking isotretinoin.

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.

*A cervical shield should not be confused with a cervical cap, which is an effective secondary method of contraception.
Referring to a Gynecologist

You may want to refer your patient to a gynecologist for:

- An examination prior to starting oral contraceptive agents or a hormonal transdermal patch
- Insertion of an IUD or hormonal vaginal ring
- Fitting a diaphragm or a cervical cap
- More detailed explanation of contraception options

You should also ask for gynecologic consultation under the following circumstances:

- Your patient’s history is suggestive of polycystic ovary syndrome (Stein-Leventhal syndrome). In addition to acne she may have:
  - Excessive facial hair growth (common when acne is present)
  - Obesity
  - Amenorrhea (no menstrual period) or irregular, heavy bleeding
  - Anovulation
- Your patient has irregular menses, possibly related to pregnancy; an eating disorder; or endometriosis. It is important to weigh your patient. Patients with eating disorders may:
  - Not admit to the problem
  - Be very underweight
- There are indications of sexual abuse found during the physical examination or counseling session.
- There is history or symptoms of sexually transmitted infection.

Obtaining a Sexual And Behavioral History

There are several reasons to take a sexual and behavioral history. You need to know about sexual promiscuity, risk-taking behavior, reactions to previous contraceptive medication, and current contraceptive practices to assess whether your patient is appropriate for the iPLEDGE Program. This information may help you eliminate unsuitable patients or refer those whose contraceptive needs require gynecologic referral.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
General Interview Information

Preparation

Ensure that your patient feels safe and comfortable.

- This is important for an effective counseling session.
- Allow time for taking the history, answering questions, and decision-making.
- A private office is more conducive to counseling than an examination room is. This may permit a more open and personal exchange.
- Interruptions by other staff members and telephone calls should be discouraged.

Use open-ended questions to encourage discussion.

- Your patient may be reluctant or embarrassed to answer questions about her sexual history.
- It may help to start asking about less sensitive material.

Being objective and non-judgmental is important in building rapport. Make sure your patient understands your questions and the information you are giving her. Listen to her use of language and tailor your language to be sure she understands.

Sexual History Questions

1. Does she menstruate? Does she menstruate regularly?
   - Most females (95%) have their menstrual period every 21 to 35 days and usually in a recurrent and regular pattern. A female whose menses vary by a week or more from month to month or vary in length or quantity of flow would qualify as irregular.

2. Has she had a hysterectomy or oophorectomy?

3. Is she still menstruating?

4. Is she postmenopausal?

5. Is she sexually active?
   - If not, is there any possibility of a sexual relationship developing?

6. If she is sexually active, are her partners men, women, or both?

7. Has she ever used contraception? Does she currently use contraception?
   - If yes, which method(s) and for how long?
   - Specifically question the use of unacceptable methods such as the progesterone-only mini-pills or female condom.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
8. If she uses oral contraceptives, does she take them exactly as prescribed? If so, which brands?

9. Does she use a secondary method of contraception every time she has sex? If so, which method?

10. How many sexual partners has she had in the past 6 months? How many sexual partners does she currently have?

11. How long has she been with her current partner(s)? Is she monogamous?

12. Has she ever had a sexually transmitted infection? Has she ever been sexually abused?

13. Has she ever been pregnant? Does she have children?

14. Has she ever had an unintended pregnancy? What was the outcome?

**Behavioral History Questions**

1. Does she engage in risk-taking behavior, such as using drugs or alcohol?

2. How is she doing in school/at work?

3. How is her relationship with her parents? With her siblings?

4. What is her cohabitational status? Is she married? Living with a partner?

5. Is she currently using any prescription or non-prescription medications, herbal supplements, or vitamins?

**Additional Guidance For Interviewing an Adolescent*  
This section offers guidance on how to approach an adolescent to obtain a sexual and behavioral history, taking into consideration concerns adolescents have about independence, parental oversight, and privacy.

**Discuss Confidentiality First**

- Inform the patient that she has a private and privileged relationship with you.
- Identify restrictions for which you may need to breach confidentiality, such as reporting physical or sexual abuse to health authorities.
- Tell her that you will not talk with her parent or parents about something she has said without discussing it with her first.

Additional Guidance For Interviewing an Adolescent (Cont.)

Start Gently When Asking About Personal History

- Start with non-threatening topics and gradually move to more sensitive issues.
- Explain that you ask all of your patients about sexual activity and tell her why this information is important.
- Consider using 1 of the following questions to initiate the discussion about the patient’s sexual history.
  - Are you dating anyone?
  - Are you intimate with anyone?
  - Are you physically close with anyone?

Identify Risk Behaviors

- Leave room for discussing casual sex partners (who, for example, may not be perceived as “boyfriends”).
  - Did you choose to have sex?
  - Has anyone forced you to have sex?
- Establish the sex of partner or partners first. Do not assume heterosexual behavior.
- Ask about oral and anal sex, and describe what you mean by this, if necessary.
  - Anal intercourse may be used by some teenagers to preserve virginity and protect against pregnancy, so they may not be using their secondary methods.
- Ask about the number of partners, STIs (sexually transmitted infections), and pregnancy prevention methods used.
  - Specifically, ask which methods the patient is using.
  - Find out if they are using unacceptable methods of contraception such as the progesterone-only mini-pill, female condom, or withdrawal.

Keep The Lines of Communication Open

- Encourage adolescents to discuss these issues with their parents. You can assist the adolescent in telling her parents about her sexual activity and her need to use 2 methods of contraception for the iPLEDGE® Program.
- Congratulate the patient for showing ability to think about her sexual health and be responsible.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Contraception Reference Material

The following sections contain some pertinent details, advantages, and disadvantages of the primary and secondary methods of effective contraception. This is not complete product information. Please refer to individual product labeling for contraindications, warnings and precautions, instructions for use, adverse events, and other product-specific information.

The percentages that follow for perfect use and typical use of a contraceptive are percentages of females having an unintended pregnancy during the first year of use, expressed as “1 female in X years.” Perfect use is defined as the use of the method correctly and consistently covering every act of intercourse. Typical use reflects the practices of the average user.

Primary Methods of Contraception

The effective primary methods of birth control fall into 3 categories:

- Single Hormonal Contraceptives
- Combination Hormonal Contraceptives
- Non-Hormonal Contraceptives

None of the primary methods protect against STIs or HIV/AIDS.

Single Hormone Contraceptives (Progestin-only)

Oral contraceptives containing no estrogen (progestin-only “mini-pills” see page 52) are not an acceptable method of contraception during isotretinoin treatment.

Single hormone methods contain a progestin that can suppress ovulation, thicken cervical mucus, and produce endometrial atrophy. Accepted methods include single hormone injection, the hormonal IUD, and implantable hormones.
Single Hormone Injections

Mechanism of action: Inhibition of follicular maturation and ovulation

Rate of Unintended Pregnancies

Perfect Use: 0.2% (1 female in approximately 500 will become pregnant)
Typical Use: 6.00% (1 female in approximately 17 will become pregnant)

Contraindications

Pregnancy, unexplained abnormal vaginal bleeding, breast cancer, or significant liver problems

Instructions For Use

Single hormonal injection of a progestin every 3 months

Advantages

Some Advantages May Include:

• It works for 3 months at a time
• The patient does not need to remember to take a pill each day
• It is good for female patients who cannot take estrogen

Disadvantages

Some Disadvantages May Include:

Black Box Warning: Prolonged use of this [drug] may result in significant loss of bone density, and loss is greater the longer the drug is administered. Bone density loss may not be completely reversible after discontinuation of the drug. A female should only use this [drug] as a long-term birth control method (for example, longer than 2 years) if other birth control methods are inadequate for her.

• Does not protect against STIs or HIV/AIDS
• It can cause irregular bleeding
• It requires a healthcare professional visit for injection every 3 months
• If patient is planning to get pregnant after she finishes isotretinoin treatment, it may take up to 18 months for return of ovulation
• Isotretinoin may make single hormonal methods less effective
Hormonal Intrauterine Device (IUD)\textsuperscript{3,4}

The hormonal IUD is indicated for contraception in female patients who have had at least 1 child, are in a monogamous relationship, and are at low risk for STIs.

**Mechanism of action:** Thickening of cervical mucus preventing passage of sperm into the uterus, inhibition of sperm capacitation or survival, and alteration of the endometrium

**Rate of Unintended Pregnancies**

- **Perfect Use:** 0.2% (1 female in 500 will become pregnant)
- **Typical Use:** 0.2% (1 female in 500 will become pregnant)

**Contraindications**

- Pregnancy or suspicion of pregnancy
- Congenital or acquired uterine anomaly, including fibroids if they distort the uterine cavity
- Acute pelvic inflammatory disease (PID) or history of PID without subsequent intrauterine pregnancy
- Postpartum endometritis or infected abortion in the past 3 months
- Known or suspected uterine or cervical neoplasia or unresolved, abnormal Pap smear
- Carcinoma of the breast
- Genital bleeding of unknown etiology
- Untreated acute cervicitis or vaginitis, lower genital tract infections
- Acute liver disease or liver tumor (benign or malignant)
- Female patient or her partner has multiple sexual partners
- Conditions associated with increased susceptibility to infections with microorganisms
- Genital actinomycosis
- Previously inserted IUD that has not been removed
- History of ectopic pregnancy or condition that would predispose to ectopic pregnancy

**Instructions For Use**

The IUD is inserted by a healthcare professional. The patient should check for IUD strings often in the first few months after insertion and after each period. If the patient cannot find the strings, the strings feel shorter or longer, she can feel the IUD itself, there are any signs of symptoms of PID, or she misses a period, instruct her to call her prescriber.
Hormonal Intrauterine Device (Cont.)

Advantages

Some Advantages May Include:
- It can be used for long-term contraception (5 years) and is relatively quickly reversible (i.e., return to fertility)

Disadvantages

Some Disadvantages May Include:
- Does not protect against STIs or HIV/AIDS
- It requires insertion and removal by a healthcare professional
- Common adverse events include menstrual changes, lower abdominal pain and cramping, acne or other skin problems, back pain, breast tenderness, headache, mood changes, nausea
- Enlarged ovarian follicles have been diagnosed in about 12% of hormonal IUD users; most disappear spontaneously during 2 to 3 months of observation
- All types of IUDs may increase the risk of pelvic inflammatory disease (PID); side effects of all types of IUDs may include cramps and heavier and longer periods in the first few months after it is placed
- IUD may be expelled, often during menses
- Isotretinoin, antibiotics, St. John’s Wort, and certain anticonvulsants may make hormonal methods less effective
- IUDs may cause menstrual changes or amenorrhea
- If a pregnancy occurs, it is more likely to result in an ectopic pregnancy

Implantable Hormones

Implantable hormones (etonogestrel implant) are a long acting (up to 3 years), reversible method of progestin-only contraception. This method of contraception involves a sterile rod(s), the size of a matchstick, for subdermal insertion under the skin on the inner side of the upper arm during a minor in-office surgical procedure.

Mechanism of Action: Inhibition of ovulation, increased viscosity of the cervical mucus, and alteration in the endometrium

Rate of Unintended Pregnancies

Perfect Use: 0.05% (1 female in 2000 will become pregnant)
Typical Use: 0.05% (1 female in 2000 will become pregnant)

Contraindications
- Known or suspected pregnancy
- Current or past history of thrombosis or thrombotic disorders

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
- Hepatic tumors (benign or malignant), active liver disease
- Undiagnosed abnormal genital bleeding
- Known or suspected carcinoma of the breast or personal history of breast cancer
- Hypersensitivity to any of the components of the implant

### Advantages

**Some Advantages May Include:**

- Effective birth control for up to 3 years
- The patient does not need to remember to take a pill each day
- Fertility may return quickly when implant is removed
- Can be used in patients who cannot take estrogen

### Disadvantages

**Some Disadvantages May Include:**

- Implant does not protect against STIs or HIV/AIDS
- May cause irregular and unpredictable bleeding or amenorrhea
- Other side effects can include headache, acne, dysmenorrhea, and emotional lability
- Associated with an increased risk of myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gall bladder disease
- Complications of insertion can include: swelling, redness, pain, bruising, scarring, infection, paresthesias, bleeding, and hematoma
- Complications of removal include: a broken rod, scar tissue making removal more difficult
- Rarely, it can be difficult or impossible to remove which may result in a surgical procedure
- If pregnancy occurs, there is a higher chance of an ectopic pregnancy
- Ovarian cysts that usually disappear spontaneously
- Studies were not done in women who weighed more than 130% of their ideal body weight or patients who are chronically taking medication that induces liver enzymes, and it is possible that the implant may be less effective in women who are overweight
- Isotretinoin, antibiotics, and St. John’s Wort may make hormonal methods less effective

If you use an implant, always verify its presence in the patient’s arm immediately after insertion by palpation. Until you confirm proper insertion, your patient must use a non-hormonal contraceptive method and is not eligible to start isotretinoin.
Combination Hormonal Contraceptives

Combination hormonal contraceptives include combination oral contraceptives, the transdermal patch, the vaginal ring, and hormonal implants. They use estrogen and a progestin in combination to suppress ovulation. In general, these methods have similar contraindications and adverse event profiles.

Mechanism of Action: Inhibition of ovulation

Contraindications

- Thrombophlebitis disorders, history of deep vein thrombosis (DVT), or thromboembolic disorder
- Cerebral vascular or coronary artery disease
- Migraine with focal aura
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior pill use
- Acute or chronic hepatocellular disease with abnormal liver function
- Hepatic adenomas or carcinomas
- Known or suspected pregnancy
- Hypersensitivity to product
- Smoking and over the age of 35
Hormonal Combination Oral Contraceptives

With perfect use, the failure rate for combination oral contraceptives is equal to that of the best currently available contraceptive measure. With typical use, oral contraceptives have the highest failure rate of the effective primary methods (Table 1). Do not prescribe combination oral contraceptives for patients whom you do not think will take them exactly as prescribed. Other primary methods that do not require daily action by the patients, such as an IUD, may be a better choice for reducing the likelihood of pregnancy.

Note: Progesterone-only contraceptives (mini-pill) are not acceptable for the iPLEDGE Program because they are not an effective method of birth control. If your patient is using them, she will have to choose another effective primary method of birth control.

Rate of Unintended Pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)
Typical Use: 9.00% (1 female in approximately 11 will become pregnant)

Additional Warnings

- Female patients with significant hypertension should not be started on oral contraceptives.
- Female patients who have had major surgery with immobilization or any leg surgery should not be started on oral contraception.
- Cigarette smoking increases the risk of serious cardiovascular adverse events with oral contraceptives. Female patients who use oral contraceptives should be strongly advised not to smoke. The risk increases with age and with the number of cigarettes smoked.
- Increased risk of venous thromboembolism and stroke

Instructions For Use

- Once daily for hormone pills for a specified time period, often followed by placebos for a specified number of days. The patient should take oral contraceptives exactly as prescribed.

Missed pill(s):

- Missed more than 2 pills: instruct the patient to call as soon as she realizes that she has missed 2 or more pills; she should be evaluated for possible emergency contraception, depending on her sexual activity. The patient should be counseled not to have intercourse for the rest of the cycle.
Hormonal Combination Oral Contraceptives (Cont.)

Advantages
Some Advantages May Include:
- May decrease the risk of the following:
  - endometrial and ovarian cancer
  - functional ovarian cysts
  - pelvic inflammatory disease
  - benign breast disease
  - ectopic pregnancy
- May decrease the incidence of dysmenorrhea and acne
- Some patients have more regular, lighter, and shorter periods

Disadvantages
Some Disadvantages May Include:
- Combination oral contraceptives do not protect against STIs or HIV/AIDS
- Common adverse events include breakthrough bleeding, nausea and vomiting, and headaches
- Associated with an increased risk of myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease
- Less effective with medications affecting hepatic metabolism such as anticonvulsants; may be less effective with the antibiotics rifampin and griseofulvin*; possible interaction with St. John’s Wort
- Isotretinoin may make hormonal methods less effective
- If pills are skipped or missed, the risk of pregnancy is very high

Hormonal Transdermal Patch

Rate of Unintended Pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)
Typical Use: 9.00% (1 female in approximately 11 will become pregnant)

Instructions For Use

The hormonal skin patch is a thin, plastic patch the female patient puts on her skin which releases birth control hormones.

One patch is used per week for 3 consecutive weeks. The patch is replaced on the same day of the week. The fourth week is patch-free. Menses occurs at this time.

If the female patient is starting the patch for the first time, she should wait until the day she begins her menstrual period.

Slipped or missed patches:

- If the patch falls off or is partially detached for less than 24 hours, the patient can reapply in the same place. Otherwise, replace with a new patch immediately. Change patches on the original schedule.
- If the patch is detached for more than 1 day or the patient is not sure how long the patch was detached, she should start a new cycle with a new change day by applying a new patch. It will not be effective for contraception for the first week.
- The patient should be instructed not to have intercourse during this first week.

Advantages

Some Advantages May Include:

- The patient does not need to remember to take a pill each day
- Some female patients have more regular, lighter, and shorter periods
- Fertility returns quickly when the patch is stopped

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Less effective in female patients over 198 pounds
- Not effective if it becomes loose or falls off for more than 24 hours or if the same patch is left on the skin for more than 1 week
- Has the same labeling for contraindications, warnings, and precautions as oral contraceptives
- Common side effects include breakthrough bleeding, nausea, headaches, and breast tenderness
- Isotretinoin, antibiotics, St. John’s Wort, and certain anticonvulsants may make hormonal methods less effective
- Possible increased risk of blood clots
Hormonal Vaginal Ring

Rate of Unintended Pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)
Typical Use: 9.00% (1 female in approximately 11 will become pregnant)

Instructions For Use

The hormonal vaginal ring is a small flexible ring containing birth control hormones which is placed into the vagina and changed once a month.

Patient inserts ring in the vagina, where it should remain for 3 weeks. She removes ring for 1 week to bring on menses. A new ring is used each month for continuous contraception.

Advantages

Some Advantages May Include:

- The patient does not need to remember to take a pill each day
- It does not need to be fitted by a clinician
- Some female patients have more regular, lighter, and shorter periods
- Fertility returns quickly when the ring is stopped

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- The ring cannot be used with a diaphragm or cervical cap
- Some female patients may have trouble inserting the ring
- It has the same labeling for contraindications, warnings, and precautions as oral contraceptives
- Efficacy of the ring is lessened if:
  - The unopened package containing the ring is put into direct sunlight or exposed to very high temperatures
  - It slips out of the vagina and is not replaced in 3 hours
  - It does not stay in the vagina for 3 weeks
  - It is left in the vagina for more than 3 weeks
- Common side effects include breakthrough bleeding, nausea and vomiting, and headaches
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal methods less effective

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Non-hormonal Contraceptives\textsuperscript{3,8}

Accepted non-hormonal methods of contraception include the copper IUD, tubal sterilization, and partner’s vasectomy. These non-hormonal methods do not protect against STIs or HIV/AIDS.

Copper IUD

The copper IUD is made of polyethylene covered with copper.

\textbf{Mechanism of Action:} Prevents fertilization by altering tubal and uterine transport of sperm

\textbf{Rate of Unintended Pregnancies}

- Perfect Use: 0.6\% (1 female in approximately 166 will become pregnant)
- Typical Use: 0.8\% (1 female in 125 will become pregnant)

\textbf{Contraindications}

- Pregnancy or suspicion of pregnancy
- Abnormalities of the uterus resulting in distortion of the uterine cavity
- Acute pelvic inflammatory disease (PID) or a history of PID
- Postpartum endometritis or infected abortion in the past 3 months
- Known or suspected uterine or cervical malignancy, including unresolved, abnormal Pap smear
- Genital bleeding of unknown etiology
- Untreated acute cervicitis or vaginitis, including bacterial vaginosis, until infection is controlled
- Diagnosed Wilson’s disease
- Known allergy to copper
- Female patient or her partner has multiple sexual partners
- Genital actinomycosis
- A previously inserted IUD that has not been removed

\textbf{Instructions For Use}

Patient should check for IUD strings often in first few months after insertion and after each period. If patient cannot find the strings, the strings feel shorter or longer, she can feel the IUD itself, there are any signs of symptoms of PID, or she misses a period, she should call her prescriber.
Copper IUD (Cont.)

Advantages

Some Advantages May Include:

• Female patients who cannot take hormones can use it
• It can be used for long-term contraception (10 years) and is relatively quickly reversible (i.e., return to fertility)

Disadvantages

Some Disadvantages May Include:

• Does not protect against STIs or HIV/AIDS
• It requires insertion and removal by a healthcare professional
• It should be used in female patients who are not at risk for STIs
• All types of IUDs may increase the risk of pelvic inflammatory disease (PID)
• Side effects of all types of IUDs may include cramps, and heavy, longer periods
• The IUD may be expelled, often during menses
Tubal Sterilization

Tubal sterilization may be accomplished using a variety of techniques. They are all considered to be very effective, virtually permanent methods of pregnancy prevention and, with the exception of hysteroscopic tubal sterilization, are immediately effective. For purposes of the iPLEDGE Program, a patient should not be permitted to consider her hysteroscopic tubal sterilization as an accepted method of contraception unless she has had a confirmatory hysterosalpingogram (HSG) or other confirmation.

**Mechanism of Action:** Tubal sterilization is the closing off of the fallopian tubes to prevent the egg from moving down the fallopian tube to the uterus and to prevent the sperm from reaching the egg.

**Rate of Unintended Pregnancies**

- Perfect Use: 0.5% (1 female in 200 will become pregnant)
- Typical Use: 0.5% (1 female in 200 will become pregnant)

**Advantages**

- Very effective, virtually permanent means of contraception

**Disadvantages**

- Does not protect against STIs or HIV/AIDS
- Difficult to reverse
- Requires surgery
- If a pregnancy does occur, there is an increased risk of an ectopic pregnancy
**Male Vasectomy**

A male's vasectomy which involves the mechanical blocking of the vasa deferentia in males is an effective primary method of contraception. Males should have semen analysis after 15 to 20 ejaculations to be sure semen is free from sperm. If the patient has more than 1 partner, each partner must be sterilized for male sterilization to be effective as the patient’s only primary method. If the patient uses male sterilization as a primary method, she should be encouraged to choose another primary method as a second method.

**Mechanism of Action:** This procedure blocks the vasa deferentia to prevent semen from entering the seminal fluid.

**Rate of Unintended Pregnancies**

- **Perfect Use:** 0.1% (1 female in 1000 will become pregnant)
- **Typical Use:** 0.15% (1 female in approximately 666 will become pregnant)

**Advantages**

**Some Advantages May Include:**

- Very effective, virtually permanent means of contraception

**Disadvantages**

**Some Disadvantages May Include:**

- Does not protect against STIs or HIV/AIDS
- Low success rate in reversing
- Requires surgery
- Not effective right away
Secondary Methods of Contraception

Most of the secondary methods are barrier contraceptives that prevent sperm from entering the vagina (condom) or cervix (diaphragm and cervical cap). Barrier methods include the diaphragm and the cervical cap, both of which must be used with spermicide. The male latex condom can be used with or without spermicide. The vaginal sponge is a delivery system for spermicide and has spermicide embedded in it. Female condoms are not acceptable for the iPLEDGE® Program.

Diaphragms and cervical caps are barrier contraceptives that are considered moderately effective when used in combination with a spermicide. The male latex condom is a barrier contraceptive that is considered moderately effective when used with or without spermicide. The vaginal sponge is also considered moderately effective. The most important issue is whether the secondary method will be used each time the patient has intercourse. If the patient selects a secondary method as the second method of contraception, she must understand how it is used and be fully committed to using it each time she has intercourse.

Female patients under 30 and female patients who have intercourse 3 or more times per week may have a higher failure rate with vaginal secondary methods.

Note: The female condom, a thin, flexible plastic tube that covers the cervical os, is not an acceptable secondary method for the iPLEDGE Program.
Male Latex Condom Used With or Without Spermicide

If the patient does not feel she can convince her partner(s) to use a latex condom (with or without spermicide) each time they have intercourse, she would need to select another secondary method where she has the control or select a second primary method.

Rate of Unintended Pregnancies

Perfect Use: 2% when used without spermicide (1 female in 50 will become pregnant)
Typical Use: 18% when used without spermicide (1 female in 6 will become pregnant)

Male condom (latex) may be used with or without spermicide.

Instructions For Use

Unrolled onto erect penis before there is any contact with female genitals; use only water-based lubricants with latex condoms.

Advantages

Some Advantages May Include:

• Protects against STIs and HIV/AIDS
• Easy to buy, no doctor/prescriber appointment needed, no pelvic exam needed
• Easy to tell when it breaks or slips, important for seeking emergency contraception
• May lower risk of cervical dysplasia and cancer

Disadvantages

Some Disadvantages May Include:

• Condoms can break or slip during sex
• May decrease sensitivity and spontaneity, may have trouble maintaining erection
• Must remember to use every time
Diaphragm Used With Spermicide\textsuperscript{3,10}

**Rate of Unintended Pregnancies**

- **Perfect Use:** 6% when used with spermicide (1 female in approximately 17 will become pregnant)
- **Typical Use:** 12% when used with spermicide (1 female in approximately 8 will become pregnant)

**Description**

- Dome-shaped rubber cap with a flexible rim available in many sizes (50-95 mm diameter) and different styles

**Additional Warnings**

- There is an association between Toxic Shock Syndrome (TSS) and diaphragm use.
- A diaphragm must be removed after 6 to 8 hours to decrease the risk of TSS.
- There may be increased risk of urinary tract infections, candidiasis, or bacterial vaginosis.
- A diaphragm may cause allergic reactions in females sensitive to latex or rubber.

**Advantages**

**Some Advantages May Include:**

- Female patients can easily carry a diaphragm with them and have control of its use
- Immediately effective
- No hormones
- No interruption of sex play; can be inserted any time before intercourse and must stay in place for at least 6 to 8 hours after intercourse; a diaphragm should not be worn for more than 24 hours
- May lower risk of cervical dysplasia and cancer
- Can be used during a menstrual period

**Disadvantages**

**Some Disadvantages May Include:**

- Does not protect against STIs or HIV/AIDS
- Requires a prescription, pelvic examination, and periodic refitting; lasts about 1 to 2 years
- Some female patients find it hard to insert
- Spermicide must be inserted in the vagina if there is repeated intercourse
- Can get pushed out of place during sex
- Must be checked for holes after sex and cleaned after use
Cervical Cap Used With Spermicide\textsuperscript{3,11}

Rate of Unintended Pregnancies in Nulliparous Females

- Perfect Use: 9\% when used with spermicide (1 female in approximately 11 will become pregnant)
- Typical Use: 20\% when used with spermicide (1 female in 5 will become pregnant)
- The failure rate is double in parous females.

Description

- Deep rubber cap with firm rim and a groove inside the rim that fits snugly around the cervix

Advantages

Some Advantages May Include:

- Same as diaphragm
- No need to add more spermicide if female patient has repeated intercourse
- Continuous protection for 48 hours

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Some female patients find it harder to insert than a diaphragm
- It cannot be used during a menstrual period
- Patient needs a prescription and a pelvic examination to fit a cervical cap; a cap lasts about 1 year
- Must be checked for holes and tears after sex and cleaned after use
- Less effective with multiparous females

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Vaginal Sponge (Contains Spermicide)$^{3,12}$

Rate of Unintended Pregnancies in Nulliparous Females

- Perfect Use: 9% (product contains spermicide) (1 female in approximately 11 will become pregnant)
- Typical Use: 12% (product contains spermicide) (1 female in approximately 8 will become pregnant)

The failure rate is double in parous females.

Description

Soft, disposable, non-abrasive polyurethane foam that is a delivery system for 1 gram of the spermicide nonoxynol-9

Advantages

Some Advantages May Include:

- Female patients can easily carry a vaginal sponge with them and have control of its use
- Immediately effective
- No hormones
- No interruption of sex play; can be inserted any time before intercourse and is effective for up to 24 hours
- No need to put in more spermicide with repeated intercourse
- No special fitting, available over the counter
- Not associated with TSS

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Less effective with multiparous females
Emergency Contraception³

Emergency contraception is indicated after sex without adequate protection:

- No contraception is used
- A secondary method slips or breaks
- Missed pill or injection
- Rape

Hormonal Emergency Contraception Pills (ECPs)

Emergency contraception is available without a prescription regardless of age. Patients must understand that the sooner ECPs are started, the more likely they are to be effective. Common side effects include nausea and vomiting. Consider prescribing medication to reduce these side effects.

Always consult complete Prescribing Information for any medications prescribed or currently being taken by your patient.

Reporting a Pregnancy

The iPLEDGE® Program Pregnancy Registry

The iPLEDGE Program Pregnancy Registry collects data on pregnancies that occur in female patients who become pregnant while taking isotretinoin or within 30 days of their last dose. Data from the registry are reported to the FDA and are used to assess the effectiveness of the iPLEDGE Program. The data are also used to evaluate further ways to reduce fetal exposure. Information gathered in the iPLEDGE Program Pregnancy Registry will be used for statistical purposes only and will be held in the strictest confidence.

The prescriber must report to the iPLEDGE Program Pregnancy Registry any pregnancy case that he/she becomes aware of while the female patient is on isotretinoin or 1 month after the last dose. Report a pregnancy by calling 1-866-495-0654. Select the option to “Report a Pregnancy.” All pregnancies should also be reported to the FDA via the MedWatch number: 1-800-FDA-1088.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
References

1. Isotretinoin Prescribing Information, 2015.

Depo-Provera® is a registered trademark of Pharmacia & Upjohn Corporation.
Mirena® is a registered trademark of the Bayer Oy Corporation.
NuvaRing® is a registered trademark of Merck Sharp & Dohme B.V.
OrthoEvra® is a registered trademark of Ortho-McNeil Pharmaceutical, Inc.
Today® Sponge is a registered trademark of Alvogen Group, Inc.
Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.
WARNING
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Recognizing Psychiatric Disorders in Adolescents And Young Adults

A guide to recognizing psychiatric disorders in adolescents and young adults for prescribers of isotretinoin
NOTES:
Be Prepared, Be Protected
VIDEO SCRIPT

SCENE 1: ABSTINENCE

FEMALE 1: I thought I was abstinent. I guess I didn’t know what abstinence really means. Now I do.

ANNOUNCER: It’s important to know what abstinence means. Not having sex. Not once, twice, or ever. Just because you’re not having sex now, doesn’t mean you will have always be abstinent. You’re only abstinent if you know you won’t be tempted to have sex. And this becomes especially important when you are taking a drug that may cause birth defects to your unborn baby. Think about it: Are you really abstinent?

SCENE 2: UNPREPARED PREGNANCY

FEMALE 2: I can’t believe I’m pregnant. It was just that one time. And I have been so careful. This can’t be right.

ANNOUNCER: You have to be sure if you are having sex at any time you can’t use any excuses. It doesn’t matter if your periods are irregular, or if you think you can’t get pregnant, or if you don’t have sex frequently. And if you are on a medication that could be harmful to your unborn baby, you need to be especially and extremely careful. Once can be enough.
SCENE 3: WITHDRAWAL

FEMALE 3: We used withdrawal for a long time. But this time withdrawal just didn’t work.

ANNOUNCER: Withdrawal is unreliable. Use effective birth control such as the contraceptive pill, diaphragm, condom, and if you are taking a medication that may cause birth defects to your unborn baby, use a combination of two. If you don’t like the pill, you have other options such as long lasting contraceptive implants, injectables, and intrauterine devices—IUDs. Always practice safe birth control using reliable effective methods to avoid pregnancy.

SCENE 4: BEING UNPREPARED

FEMALE 4: This is so nice. (Thoughts of Female 4) I didn’t think this would happen. I mean at least not tonight. I’m so surprised and unprepared.

ANNOUNCER: Be prepared and protected. Think about it before hand. You may have sex and you might get pregnant? Don’t assume your partner will take responsibility. And if you are on a medication that may cause birth defects—think about your unborn baby. Be prepared and ready to use reliable effective forms of birth control.
SCENE 5: BIRTH CONTROL CAN FAIL

FEMALE 5: I can’t believe this. There’s a hole in my diaphragm. What if I get pregnant? What am I going to do?

ANNOUNCER: Your doctor or nurse can help you find out if you are really pregnant. If you are, they can give you advice. Always make sure your birth control is reliable and effective. And if you are on a drug that may cause birth defects, be sure you are doubly protected.

If you have any questions you should speak to your doctor or nurse. Carefully follow instructions provided by your prescriber, and consult with them if you have any questions about pregnancy, birth control, or your medical treatment.

Frame 1:
Complete Contraceptive Certainty = Be prepared Be protected

Frame 2:
You have just seen five scenarios with the most common reasons women have unwanted or ill-timed pregnancies.

Frame 3:
If you are not being completely abstinent, then
- Use birth control regularly
- Use the most effective types of birth control
- Be sure the method you choose is reliable
- Be prepared and be protected
Frame 4:

Brought to you as an educational service.
Be Aware Video Script

**Opening Segment**
“ISOTRETINOIN CANNOT BE TAKEN BY WOMEN WHO ARE PREGNANT, BECAUSE ISOTRETINOIN CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY.

In this video we will see what can happen to an unborn baby if the baby’s mother takes isotretinoin.

A woman must not take isotretinoin at any time during pregnancy.

**Storyboard P2**
Isotretinoin is usually prescribed for males and females to treat the most severe form of acne called nodular acne. This type of acne cannot be cleared up by any other acne treatments, including antibiotic pills. Nodular acne has many red, swollen, tender lumps that form in the skin. These lumps are the size of a pencil eraser or larger and can result in permanent scars if not treated.

Because of serious side effects and birth defects, patients should use isotretinoin only if other treatments including antibiotic pills have not worked.

**Storyboard P3**
“FEMALE PATIENTS MUST NOT TAKE ISOTRETINOIN IF THEY ARE PREGNANT, PLAN TO BECOME PREGNANT OR BECOME PREGNANT DURING THERAPY. TO AVOID PREGNANCY, WOMEN MUST USE TWO FORMS OF EFFECTIVE CONTRACEPTION ONE MONTH BEFORE STARTING ISOTRETINOIN, WHILE TAKING ISOTRETINOIN, AND FOR ONE MONTH AFTER STOPPING ISOTRETINOIN UNLESS THEY ARE ABSOLUTELY ABSTINENT, NEVER HAVING SEX, OR HAVE HAD THEIR UTERUS OR WOMB REMOVED”.

**Storyboard P4**
“ISOTRETINOIN CAPSULES BREAK DOWN IN THE BODY AND THE MEDICINE ENTERS INTO THE BLOODSTREAM

**Storyboard P5**
“AND THE BLOOD IS CARRIED INTO THE PLACENTA WHERE IT REACHES THE UNBORN FETUS.
The medicine can cause severe birth defects.”

**Storyboard P6**
“It is highly possible that the unborn baby may die because the baby’s mother took isotretinoin.”

**Storyboard P7**
“If the fetus lives, as the fetus develops, several birth defects can begin to take place.

These birth defects may be caused by taking isotretinoin during pregnancy”.

**Storyboard P8**
“One of these birth defects may be abnormal skull development”. “Use of isotretinoin during pregnancy may cause an under development or over development of the skull”.

**Storyboard P9**
“Development of the ears may also be affected”. “The ears may not fully develop if isotretinoin is used during pregnancy. The outer ear may be deformed and the ear canal may be very small or absent entirely causing deformity”.

**Storyboard P10**
“The eyes also may not develop fully”.
“The eye socket may be very small or not develop at all causing facial deformity

**Storyboard P11**
“As face structure begins to form the fetus can have a flattening of the nose and a twisting of the mouth. These birth defects could happen from using isotretinoin during pregnancy”.

**Storyboard P12**
“The baby may also be born with a separation of the roof of the mouth and sometimes the lips which is known as a cleft palate”.

**Storyboard P13**
IN ADDITION TO THE VISIBLE DEFECTS, SEVERAL INTERNAL SERIOUS AND LIFE-THREATENING BIRTH DEFECTS MAY DEVELOP IN THE HEART AND IN THE ENTIRE HEART AND BLOOD FLOW SYSTEM.

One of these defects can include an abnormal heart that has the arteries and veins in the wrong position.

**Storyboard P14**
“The system that helps to fight infection may also be affected. One of the glands in this system - the thymus gland may not develop and the baby then would have trouble fighting infections.” “In addition, another gland -the parathyroid gland may not develop. The parathyroid gland helps the baby to form bones by controlling the amount of calcium in the body.

**Storyboard P15**
Brain and nervous system defects including an abnormal brain may occur…” OR AN UNDERDEVELOPMENT OF THE BRAIN. IT HAS ALSO BEEN REPORTED THAT SOME CHILDREN HAVE LOW IQ SCORES”. 

Reference ID: 4252185
In summary, taking isotretinoin during pregnancy can result in any or all of these birth defects:

- The skull may over- or under-develop.
- FACIAL DYSMORPHIA CAN OCCUR, CAUSING A FLATTENING OF THE NOSE AND DISTORTION OF FACIAL STRUCTURE.
- Enlargement of the brain may occur.
- Eye sockets may be very small or not develop at all.
- The brain can also under-develop.
- Ears may not fully develop.
- The thymus gland may not develop, affecting an infant’s ability to fight off disease.
- Abnormalities in the heart and entire cardiac system can be life threatening.
- A cleft palate may form.

UNLIKE THE BIRTH DEFECTS THAT ARE SEEN IN THE BABIES WHEN MOTHERS TAKE ISOTRETINOIN, THERE IS NO PATTERN OF BIRTH DEFECTS WHEN FATHERS TAKE ISOTRETINOIN.

“But men who take isotretinoin should be careful in other ways.” Men might not realize that they should not donate blood during, and for a period of one month following, the end of their isotretinoin treatment”.

“As discussed earlier, isotretinoin is carried through the bloodstream and a pregnant woman could, unknowingly accept a blood transfusion from a man or a woman who took isotretinoin. The blood and medicine could then pass into the placenta possibly harming an unborn baby”.

Therefore, it is extremely important that both men and women taking isotretinoin do not donate blood during treatment and for a period of at least one month following the end of their isotretinoin treatment.

“Neither men nor women should ever share their isotretinoin with another woman…”

“...BECAUSE OF THE RISK THAT SHE MAY BE PREGNANT.”

“No one should ever share any medicine with anyone else, because the medicine may harm the other person.”
**Black Box**
YOU MUST NOT BECOME PREGNANT WHILE TAKING ISOTRETINOIN, OR FOR ONE MONTH AFTER YOU STOP TAKING ISOTRETINOIN.

Isotretinoin can cause severe birth defects in babies of women who take it while they are pregnant, even if they take isotretinoin for only a short time.

There is an extremely high risk that your baby will be deformed or will die if you are pregnant while taking isotretinoin. Taking isotretinoin also increases the chance of miscarriage and premature births.

Female patients will not get their first prescription for isotretinoin unless there is proof they have had two negative pregnancy tests. The first test must be done when your prescriber decides to prescribe isotretinoin. The second pregnancy test must be done during the first five days of the menstrual period right before starting isotretinoin therapy, or as instructed by your prescriber. Each month of treatment, you must have a negative result from a urine or serum pregnancy test. Female patients cannot get another prescription for isotretinoin unless there is proof that they have had a negative pregnancy test.

WHILE YOU ARE TAKING ISOTRETINOIN, YOU MUST USE EFFECTIVE BIRTH CONTROL. YOU MUST USE 2 SEPARATE, EFFECTIVE FORMS OF BIRTH CONTROL AT THE SAME TIME FOR AT LEAST ONE MONTH BEFORE STARTING ISOTRETINOIN, WHILE YOU TAKE IT, AND FOR ONE MONTH AFTER YOU STOP TAKING IT. YOU CAN EITHER DISCUSS EFFECTIVE BIRTH CONTROL METHODS WITH YOUR PRESCRIBER OR GO FOR A FREE VISIT TO DISCUSS BIRTH CONTROL WITH ANOTHER PHYSICIAN OR FAMILY PLANNING EXPERT. YOUR PRESCRIBER CAN ARRANGE THIS FREE VISIT, WHICH WILL BE PAID FOR BY THE MANUFACTURER.

You must use two separate forms of effective birth control because any method, including birth control pills and sterilization, can fail. There are only 2 reasons that you would not need to use 2 separate methods of effective birth control:

1. You have had your womb removed by surgery— a hysterectomy or
2. You are absolutely certain you will not have genital-to-genital sexual contact with a male before, during and for one month after isotretinoin treatment.

IF YOU HAVE SEX AT ANY TIME WITHOUT USING TWO FORMS OF EFFECTIVE BIRTH CONTROL, GET PREGNANT, OR MISS YOUR PERIOD, STOP USING ISOTRETINOIN AND CALL YOUR PRESCRIBER RIGHT AWAY.
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.
CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate.

Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately, and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

SPECIAL PRESCRIBING REQUIREMENTS

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE®. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program (see PRECAUTIONS).
WARNINGS
Psychiatric Disorders: Isotretinoin may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. No mechanism of action has been established for these events (see ADVERSE REACTIONS: Psychiatric). Prescribers should read the brochure, Recognizing Psychiatric Disorders In Adolescents And Young Adults: A Guide For Prescribers Of Isotretinoin. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin therapy, patients and family members should be asked about any history of psychiatric disorder, and at each visit during therapy patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary. Signs and symptoms of depression, as described in the brochure Recognizing Psychiatric Disorders In Adolescents And Young Adults, include sad mood, hopelessness, feelings of guilt, worthlessness or helplessness, loss of pleasure or interest in activities, fatigue, difficulty concentrating, change in sleep pattern, change in weight or appetite, suicidal thoughts or attempts, restlessness, irritability, acting on dangerous impulses, and persistent physical symptoms unresponsive to treatment. Patients should stop isotretinoin and the patient or a family member should promptly contact their prescriber if the patient develops depression, mood disturbance, psychosis, or aggression, without waiting until the next visit. Discontinuation of isotretinoin therapy may be insufficient; further evaluation may be necessary. While such monitoring may be helpful, it may not detect all patients at risk. Patients may report mental health problems or family history of psychiatric disorders. These reports should be discussed with the patient and/or the patient’s family. A referral to a mental health professional may be necessary. The physician should consider whether isotretinoin therapy is appropriate in this setting; for some patients the risks may outweigh the benefits of isotretinoin therapy.

Pseudotumor Cerebri: Isotretinoin use has been associated with a number of cases of pseudotumor cerebri (benign intracranial hypertension), some of which involved concomitant use of tetracyclines. Concomitant treatment with tetracyclines should therefore be avoided. Early signs and symptoms of pseudotumor cerebri include papilledema, headache, nausea and vomiting, and visual disturbances. Patients with these symptoms should be screened for papilledema and, if present, they should be told to discontinue isotretinoin immediately and be referred to a neurologist for further diagnosis and care (see ADVERSE REACTIONS: Neurological).

ADVERSE REACTIONS
Neurological: pseudotumor cerebri (see WARNINGS: Pseudotumor Cerebri), dizziness, drowsiness, headache, insomnia, lethargy, malaise, nervousness, paresthesia, seizure, stroke, syncope, weakness
Psychiatric: suicidal ideation, suicide attempts, suicide, depression, psychosis, aggression, violent behaviors (see WARNINGS: Psychiatric Disorders), emotional instability
Of the patients reporting depression, some reported that the depression subsided with discontinuation of therapy and recurrent with reinstitution of therapy.

REPORTING ADVERSE EVENTS
Specific information about adverse events that may occur during isotretinoin therapy may be reported to the individual makers of isotretinoin and/or to the Food and Drug Administration MedWatch Program at 1-800-FDA-1088 or via www.fda.gov/medwatch/report.htm.
The contact information for specific brands of isotretinoin can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.

ISOTRETINOIN
Isotretinoin is a retinoid related to vitamin A. Patients should be advised against taking vitamin supplements containing vitamin A to avoid additive toxic effects.
Introduction

Mental health problems are underdiagnosed and undertreated. Dermatologists and other isotretinoin prescribers often see patients who are otherwise healthy, and they may be among the only professionals who have opportunities to evaluate patients’ mental health. Healthcare providers who recognize the signs and symptoms of psychiatric illness and respond appropriately can improve, and perhaps even save, their patients’ lives.

Isotretinoin may cause depression, psychosis, and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. Although causality has not been established for these reports, awareness of signs and symptoms may save your patient’s life. This brochure provides an overview of depression. The goal of this brochure is to help you identify when a psychiatric consult is advisable.

You and your staff may feel uncomfortable evaluating your patients’ mental health status. It is often difficult to distinguish clinical depression from other responses. It may also be difficult to decide whether erratic behavior may warrant psychiatric evaluation, especially if that behavior seems to be age-appropriate in a teenager. However, as with any specialized problem, you may identify patients who seem to need more than dermatologic care, and you may need to refer them to a specialist. Knowing when to make a referral for a patient who may be at psychiatric risk can make a major difference in the patient’s life. In extreme cases, it can mean the difference between life and death.

Depression

Depression and suicidal tendencies are 2 important psychiatric conditions that may be observed in dermatology and family practice settings. This brochure provides an overview of depression because depression is the most commonly reported psychiatric adverse event in patients taking isotretinoin and is also a well-established risk factor for suicidal behavior.

Depression is characterized by symptoms that include intense, persistent sadness; anxiety; loss of pleasure from usual activities; and loss of energy. These feelings can be normal responses to a negative life event, but clinical depression is either not triggered by such an event or is disproportionate to the trigger.

Depression can be episodic. According to the National Comorbidity Survey, 16.2% (between 32.6 and 35.1 million) of Americans will experience depression at some point during their lives, and 6.6% (between 13.1 and 14.2 million) are depressed in any given month. Several epidemiological studies reported that up to 8.3% of adolescents in the United States suffer from depression. Older adolescents experience more depressive symptoms than adults and comparable symptom persistence, suggesting that these adolescents may be at the highest risk for depression.
Depression (Cont.)
Depression can take several forms: 3 of the most common are dysthymia, major depression, and bipolar disorder. These 3 disorders are characterized by various combinations of the symptoms listed in Table 1. Not every patient exhibits all depressive symptoms. Some patients, especially adolescents, may display irritability instead of sadness.

TABLE 1. Symptoms of Depression

- Persistent sad, anxious, or “empty” mood
- Feelings of hopelessness, pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy, fatigue, being “slowed down”
- Difficulty concentrating, remembering, making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight loss or overeating and weight gain
- Thoughts of death or suicide; suicide attempts
- Restlessness, irritability
- Persistent physical symptoms that do not respond to treatment, such as headaches, digestive disorders, and chronic pain
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real


Dysthymia has characteristics similar to those of major depression but is not as disabling. People with dysthymia often function adequately but not at previous wellness levels, and are at risk for episodes of major depression. In major depression, a combination of symptoms prevents the patient from working, studying, and/or engaging in normal activities.
In bipolar disorder, the patient alternates between periods of depression (severe lows) and episodes of mania (severe highs).2

**Symptoms of Mania**

- Abnormal or excessive elation
- Unusual irritability
- Decreased need for sleep
- Grandiose notions
- Increased talking
- Racing thoughts
- Increased sexual desire
- Markedly increased energy
- Poor judgment
- Inappropriate social behavior

**Cause of Depression**

The causes of depression are often multifactorial and may include:

- Genetic predisposition2
- Stress at home, work, or school2
- Loss of a parent or loved one8
- Alcohol or substance abuse9
- Breakup of a romantic relationship10
- Medications11

**Suicide**

Suicide accounts for more than 30,000 American deaths each year. It is the third leading cause of death (after accidents and homicide) among people aged 15 to 24, which makes it responsible for more deaths in this age group than any physical illness.12-14 Of the total number of suicides among people ages 15 to 24 in 2001, 86% were male and 14% were female.15, 16 Healthcare providers often miss the warning signs because patients may hide suicidal intent very successfully. In fact, 60% of people who commit suicide had seen a physician within 1 month of their deaths.9 Suicidal tendencies rarely arise spontaneously; 93% of people who commit suicide suffer from depression, schizophrenia, and/or substance abuse.17
Suicide (Cont.)
Up to 60% of adolescents and young adults think about suicide at some point, but fortunately these thoughts usually pass. Few people who have suicidal thoughts make the attempt, and most attempts at suicide are unsuccessful. The following are some elements of a suicide risk assessment that can be used to determine the individual’s risk level for suicide:
- Ideation (thoughts of death or suicide)
- Suicidal intent
- Plan (specific time, place, and method)
- Means (e.g., a firearm in the house or a supply of drugs)

Women are twice as likely as men to attempt suicide, but men are 4 times more likely to be successful. Women usually use means from which they may be rescued, such as a drug overdose, whereas men tend to use firearms or automobiles. Firearms are used in 55% of all completed suicides.

Despite a patient’s attempt to hide suicidal thoughts, he or she may send deliberate warning signals, some of which can be explicit. Every mention or discussion of “killing myself” should be treated with utmost seriousness.

Evaluating And Referring Patients For Psychiatric Disorders
Although only 5% of the population is depressed at any given time, the incidence has been found to be closer to 15% to 20% in primary care settings. Given that 1 in 5 patients who come to your office may have some degree of depression, a few questions can identify patients who may be at risk.

Talking About Depression
Although it can be awkward to explain to a patient that he or she may have signs of depression (or any mental illness), the awkwardness can be minimized by reminding the patient that:
- Depression is very common
- It matches some of the symptoms the patient described
- It is treatable

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Assessments: Depression

While taking a history, the prescriber should suspect the likelihood of depression if the patient has symptoms such as:

- Persistent sad or irritable mood
- Loss of interest in activities once enjoyed
- Significant change in appetite or body weight
- Difficulty sleeping or oversleeping
- Psychomotor agitation or retardation
- Loss of energy
- Feelings of worthlessness or inappropriate guilt
- Difficulty concentrating
- Recurrent thoughts of death or suicide

In children and young adolescents, other signs to look for include:

- Frequent, vague, non-specific physical complaints such as headaches, muscle aches, stomach aches, or tiredness
- Frequent absences from school or poor performance in school
- Talk of or efforts to run away from home
- Outbursts of shouting, complaining, unexplained irritability, or crying
- Being bored
- Lack of interest in playing with friends
- Alcohol or substance abuse
- Social isolation, poor communication
- Fear of death
- Extreme sensitivity to rejection or failure
- Increased irritability, anger, or hostility
- Reckless behavior
- Difficulty with relationships

The prescriber should also discuss with the patient:

- Alcohol or substance abuse
- Chronic pain
- Real or perceived disfigurement

Studies indicate that acne is associated with symptoms such as social embarrassment, low self-esteem, and anxiety, but an association of acne with frank depressive disorders has not been established, nor has treatment of acne by itself been shown to ameliorate frank depressive disorders.22-24
Evaluating And Referring Patients For Psychiatric Disorders (Cont.)

Assessments: Suicide

Psychiatric specialists have identified several factors for suicide risk. These include:\n\begin{itemize}
\item Presence or history of depression, bipolar disorder, or other psychiatric disorder
\item Access to firearms in the home
\item Family history of suicide or violence, including abuse
\item Poor physical health, chronic illness, or chronic pain
\item Alcohol or substance abuse
\item Previous suicide attempt
\end{itemize}

It is important to note that depression itself is a major risk factor for suicidal behavior. Thus, special attention is needed when prescribing drugs that may cause depression. An association with isotretinoin should be considered in patients with signs and symptoms of depression, even in the presence of other life stressors. Discontinuation of isotretinoin may be insufficient intervention and a formal psychiatric evaluation should be conducted. It is also important to note that signs and symptoms of depression are not included in all reported cases of suicidal behavior. It is not known if this means the signs were masked by the patient, unrecognized by observers, or if the suicidal tendency arose impulsively. It is important that patients taking isotretinoin be made aware of this so that they might recognize any such signs and symptoms. Patients (and parents, if the patient is a minor) should be instructed to stop isotretinoin and seek immediate medical help.

Talking with patients about suicide does not encourage or remind them that suicide is an option.

Knowing When to Refer

You should refer the patient to a psychiatric specialist for further evaluation if any of the following apply:
\begin{itemize}
\item Risk factor(s) for suicide is (are) present
\item The patient has, or may have, clinical depression or bipolar disorder, or if the prescriber believes that there may be a problem but cannot classify it
\item The patient has expressed interest in, or spontaneously mentioned, suicide
\item There is any question about the patient’s safety
\end{itemize}

Summary

Prescribers who are alert to the warning signs of psychiatric disorders can guide patients to receive the help they need. Observing patients for signs of depression and suicidal ideation, and referring appropriate patients to a psychiatric specialist, need not be complicated. The benefits to patients can be immense, even life saving.
References


Reference ID: 4252185
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.
STEPS TO REQUEST AN EXEMPTION FOR FEMALE PATIENTS
WITH SERIOUS MEDICAL REASONS

Follow these steps to request an exemption from the iPLEDGE Program requirements for a female patient with serious medical reasons.

NOTE: The intent of this form is to request an exemption from the iPLEDGE Program requirements for a non-pregnant patient with serious medical reason(s) who is unable to obtain an isotretinoin prescription by completing the requirements in the iPLEDGE Program at this time. It is not intended to replace the requirements of the iPLEDGE Program.

1. Complete a new [Request for Exemption for Patients with Serious Medical Reasons] form. Print the completed form, sign and date.

2. Fax the form (all pages) to 866-486-7001.

Call 877-475-3345 if you need any assistance with the exemption request. If an agent is not immediately available, please leave contact information and the call will be returned. Please note that this phone number must only be used for requesting exemptions for patients with serious medical reasons. No other iPLEDGE questions or issues will be handled through this number.

NOTE: This form MUST be filled out and signed by the requesting prescriber. All required information (*) must be provided. Please FAX this completed form to 866-486-7001.

*Prescriber ID  "[click here and enter the prescriber's iPLEDGE ID]"

*Prescriber Name  "[click here and enter the prescriber's name]"

*Patient ID  "[click here and enter the patient's iPLEDGE ID]"

*Patient Date of Birth  "[click here and enter the patient's date of birth]"

*Office Telephone Number  "[click here and enter your telephone number]"

*Office Fax Number  "[click here and enter your fax number]"

Forms received after 8PM Eastern Time will be processed on the next business day. Forms received after 8PM Eastern Time on a Friday will be processed the following Monday (or Tuesday, if Monday is a federal holiday).
REQUEST FOR EXEMPTION
FOR PATIENTS WITH
SERIOUS MEDICAL REASONS

☐ Exemption Option 1 - Tanner Stage 1 or 2
By selecting this option I attest that all of the following apply to this patient:
  • Classified as Tanner Stage 1 (pre-pubertal female) or Stage 2 (female who has not yet experienced menarche or breast development)
  • Not considered to be of reproductive potential
  • Not currently pregnant
  • I will evaluate this patient’s reproductive status while receiving isotretinoin and I will notify the iPLEDGE Program within 10 business days of any change in the patient’s reproductive status

☐ Exemption Option 2 - Expedite Start of Treatment
By selecting this option I attest that all of the following apply to this patient:
  • Medical condition necessitates that she be exempt from the initial wait period
  • Not currently pregnant
  • Required to take monthly pregnancy tests
  • Required to successfully complete monthly comprehension testing
  • I understand that the patient will have 7 days to obtain her prescription from the date of the monthly pregnancy test specimen collection

☐ Exemption Option 3 – Cognitively and/or Physically Impaired
By selecting this option I attest that all of the following apply to this patient:
  • Medical condition necessitates that she be exempt from the initial wait period and the monthly comprehension testing
  • Not currently pregnant
  • Required to take monthly pregnancy tests
  • I understand that the patient will have 7 days to obtain her prescription from the date of the monthly pregnancy test specimen collection

Please make certain that you maintain medical documentation supporting the reason(s) for this exemption. The iPLEDGE Program may require a copy.

- The medical exemption process is governed by the iPLEDGE Non-Compliance Action Policy. Intentional misuse of the medical exemption process may result in Permanent Deactivation from the iPLEDGE Program resulting in a permanent loss of isotretinoin prescribing privilege.
- I attest that I am both qualified and have performed the necessary medical evaluation(s) to determine that the medical exemption is appropriate for this patient based on the iPLEDGE Program requirements.

* Signature ______________________________________

* Date of Request ____________________

PLEASE FAX COMPLETED COPY TO 866-486-7001

iPLEDGE
P.O. Box 29094
Phoenix, AZ 85038
Exemption Phone Number: 1-877-475-3345
Exemption Fax Number: 1-866-486-7001
iPLEDGE Call Center: 1-866-495-0654

Reference ID: 4252185
Register New Designee

Designees are office staff that are registered in the iPLEDGE Program. To register the designee, enter the designee information and click the Save and Print button.

Note: The registered prescriber is responsible for all information entered and activities performed in the iPLEDGE Program by all designees under his/her supervision.

All fields below are required unless otherwise indicated:

First Name: [Input Field]
Middle Initial (Optional): [Input Field]
Last Name: [Input Field]
Address: [Input Field]
City: [Input Field]
State: [Input Field]
Zip: [Input Field]
Phone Number: [Input Field]
Fax (Optional): [Input Field]
Email (Optional): [Input Field]
Preferred Method of Communication: [Input Field]

Save and print designee's registration:
To complete your designee's registration, click the Save and Print button below, have the designee sign the form, then mail or fax the signed form to the address or fax number on the form.

Save and Print
Register New Designee

Designees are office staff that are registered in the iPLEDGE Program. To register the designee, enter the designee information and click the Save and Print button.

Note: The registered prescriber is responsible for all information entered and activities performed in the iPLEDGE Program by all designees under his/her supervision.

All fields below are required unless otherwise indicated.

First Name

Middle Initial (Optional)

Last Name

Address

Address

Address

Address

City

State

Select

Zip

Phone Number

Fax (Optional)

Email (Optional)

Preferred Method of Communication

Select

Save and print designee’s registration

To complete your designee's registration, click the Save and Print button below, have the designee sign the form, then mail or fax the signed form to the address or fax number on the form.

Save and Print
Designee Registration

Mail To
iPLEDGE - Committed to Pregnancy Prevention
PO BOX 2904
Phoenix AZ 85038-9978

Or Fax to
1-866-495-0660

Designee Number
S2841734

Your Information:
Jeff Brevikski
7510 East Camelback Road
Scottsdale, AZ 85251
Phone 555-555-5555 Fax
Email jbrevikski@test.com
Preferred Method of Communication Email

_________________________________________  ________________________
Desginee Signature  Date

Return to Home Page
REGISTERING AND MANAGING OFFICE STAFF DESIGNEES

As a registered prescriber, you may designate a member of your office staff to perform most patient activities for you in the iPLEDGE system. An Office Staff Designee must be registered in the iPLEDGE Program and receive a unique username and password. You may assign a member of your staff as your Office Staff Designee once the registration process has been completed. A registered and designated Office Staff Designee may perform most patient activities for you in the iPLEDGE system. A registered and designated Office Staff Designee may NOT confirm the serious medical reason(s) exemption process in the iPLEDGE system on your behalf, as the confirmation requires the digital signature of a registered prescriber.

The registered prescriber is responsible for all information entered and activities performed in the iPLEDGE system by the Office Staff Designee.

Registering An Office Staff Designee

Go to www.ipledgeprogram.com and log in by entering your username (DEA number or program-generated username) and password. You will be presented with the Prescriber home page. Select the “Manage Delegates/Designees” button. The Manage Delegates and Designees page will be displayed. Select the “Register New Designee” button. The Office Staff Designee Registration form will be presented. Have the Office Staff Designee follow the registration instructions on the form to complete the registration.

Managing Office Staff Designees

Go to www.ipledgeprogram.com and log in by entering your username (DEA number or program-generated username) and password. You will be presented with the Prescriber home page. Select the “Manage Delegates/Designees” button. The Manage Delegates and Designees page will be presented. Select the “Manage Designees” button to display the Manage Designees page. On the Manage Designees page, enter the Office Staff Designee’s iPLEDGE username and select “Add.”

It is important to note the following:

- Your Office Staff Designee’s access to activities in the iPLEDGE system is dependent on your access to the system. Specifically, if you have not been activated in the system or if your activation has expired, your Office Staff Designee will not be able to perform activities in the iPLEDGE system.
- Although several prescribers may utilize the same Office Staff Designee, the Office Staff Designee only needs to register in the iPLEDGE Program once.
Prescriber Registration – For Prescribers (Button) from Public Home Page
Prescriber Registration

Attention: This registration page is for licensed prescribers only. If you are a patient, you must be registered in the PLEDGE Program by your doctor.

Create Prescriber Username

Please provide your DEA number. This will be used as your Username to identify you in the program and for you to login to the PLEDGE Program system using the phone or Internet site. The DEA number provided must be your DEA number, not an institutional or shared DEA number. Please provide only one DEA number if you have more than one.

If you do not have a DEA number, check the box indicating that you would like the program to generate a Username to be used to identify you in the program. This program-generated Username will be stopped to you in your prescriber educational kit.

DEA Number

or

Generate Username

Prescriber Contact Information

Enter or confirm your information. All fields below are required unless otherwise indicated:

First Name

Middle Name (Optional)

Last Name

Suffix (Optional)

Specialty (Optional)

Address

City

State (Optional)

Zip

Preferred Method of Communication

Email

Phone Number

Extension (Optional)

Email (Optional)

Fax (Optional)

Prescriber Identifiers

This notification is to inform you that with the launch of the REMS Pharmacy Network, the PLEDGE Program will require prescribers to provide a National Provider Identifier (NPI). If your NPI is not on file with the PLEDGE Program, you will be prompted to enter your NPI upon first log-in to the enhanced PLEDGE Program. Additionally, if you are registered with the Drug Enforcement Administration (DEA), the system will require entry of your DEA number. Failure to supply these identifiers may result in your patients' prescriptions not being authorized for dispensing.

DEA

NPI

I do not have a DEA

Select Delegates (Optional)

DEA Number or Username

Delegate List

Expiration Date (mm/dd/yyyy)

Add

Remove

Save and Print

Click the Save and Print button below. This will print a print friendly registration form for your signature. After printing and signing, return the form to the address or fax number found on the form.
Prescriber Registration

Mail To
iPLEDGE - Committed to Pregnancy Prevention
PO BOX 2994
Phoenix AZ 85068-9978

Or Fax to
1-866-495-0660

Username
AB1234567

Your information:
Jane Smith MD Derm
Scottsdale Clinic
123 Test Drive
Blue Bell, PA 18754
Phone Number 555-555-1212
Email test@aol.com
Preferred Method of Communication Email

Your delegates:
None Selected

Identifiers:
DEA - AB123456
NPI - 1234567890

__________________________  ______________________
Prescriber Signature          Date

Return to Home Page
WARNING
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately, and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

SPECIAL PRESCRIBING REQUIREMENTS

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE®. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program (see PRECAUTIONS).
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>About isotretinoin</td>
<td>4</td>
</tr>
<tr>
<td>The iPLEDGE® Program</td>
<td>6</td>
</tr>
<tr>
<td>Pharmacies and the iPLEDGE Program</td>
<td>8</td>
</tr>
<tr>
<td>The iPLEDGE web site and phone system</td>
<td>10</td>
</tr>
<tr>
<td>The Responsible Site Pharmacist</td>
<td>12</td>
</tr>
<tr>
<td>Procedure for filling and dispensing prescriptions</td>
<td>16</td>
</tr>
<tr>
<td>iPLEDGE Program general information</td>
<td>19</td>
</tr>
<tr>
<td>Additional contraception information</td>
<td>25</td>
</tr>
<tr>
<td>For more information about isotretinoin products</td>
<td>25</td>
</tr>
</tbody>
</table>
About Isotretinoin

Isotretinoin is used to treat severe recalcitrant nodular acne. Isotretinoin belongs to a class of drugs known as retinoids, commonly understood to include all natural and synthetic analogues of vitamin A. Treatment with isotretinoin should not be undertaken before conventional treatment has been tried first, including the use of systemic antibiotic therapy, and the patient has been fully counseled about the warnings and precautions in the isotretinoin package insert.

Isotretinoin is teratogenic and must not be used by pregnant women. Women should not become pregnant while taking isotretinoin or for 1 month after treatment is discontinued. A patient who becomes pregnant during treatment should stop taking isotretinoin and immediately contact her prescriber.

Isotretinoin use is associated with other potentially serious adverse events as well as more frequent, but less serious side effects. More frequent, less serious side effects include cheilitis, dry skin, skin fragility, pruritus, epistaxis, dry nose and dry mouth, and conjunctivitis.

Serious Adverse Event Warnings include psychiatric disorders* (depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors). Prescribers should read the brochure Recognizing Psychiatric Disorders in Adolescents and Young Adults: A Guide for Prescribers of Isotretinoin. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin treatment, patients and family members should be asked about any history of psychiatric disorder, and at each visit during treatment patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary.

Other Serious Adverse Events include pseudotumor cerebri; pancreatitis; hyperlipidemia; hearing impairment*; hepatotoxicity; inflammatory bowel disease; skeletal changes† (bone mineral density changes, hyperostosis, premature epiphyseal closure); and visual impairment (corneal opacities, decreased night vision).

Patients should be reminded to read the Medication Guide, distributed by the pharmacist at the time the isotretinoin is dispensed as required by law.

*No mechanism of action has been established for these events.
†The use of isotretinoin in patients 12 to 17 should be given careful consideration especially when a known metabolic or structural bone disease exists.
Pregnancy After Isotretinoin Treatment

The terminal elimination half-life of isotretinoin varies but is generally within 10 to 20 hours. The elimination half-life of one of the isotretinoin metabolites, 4-oxoisotretinoin, is approximately 25 hours. Since plasma elimination is host dependent, prescribers should warn patients not to become pregnant for 1 month post treatment. Women who become pregnant during this month should be counseled as to the outcome data. In 1989, Dai et al reported the results of an epidemiologic study of pregnancies that occurred in women who conceived after discontinuing isotretinoin. They studied women from 5 days to more than 60 days between the last dose of isotretinoin and conception. The incidence of birth defects in former isotretinoin patients was not significantly different from the rate in the general population.

Isotretinoin is found in the semen of male patients taking isotretinoin, but the amount delivered to a female partner would be about 1 million times lower than an oral dose of 40 mg. While the no-effect limit for isotretinoin-induced embryopathy is unknown, 20 years of postmarketing reports include 4 with isolated defects compatible with features of retinoid-exposed fetuses; however, 2 of these reports were incomplete, and 2 had other possible explanations for the defects observed.

Birth Defects

There is an extremely high risk that a deformed infant will result if pregnancy occurs while female patients are taking isotretinoin in any amount even for short periods of time. Potentially, any fetus exposed during pregnancy can be affected. Not every fetus exposed to isotretinoin has resulted in a deformed child. However, there are no accurate means of determining which fetus has been affected and which fetus has not been affected.

When isotretinoin is taken during pregnancy, it has been associated with fetal malformations, and there is an increased risk for spontaneous abortions and premature birth. The following human fetal abnormalities have been documented.

External abnormalities

Skull abnormality; ear abnormalities (including anotia, microtia, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate.

Internal abnormalities

CNS abnormalities including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit; cardiovascular abnormalities; thymus gland abnormalities; parathyroid hormone deficiencies. In some cases death has occurred with certain of the abnormalities noted.
The iPLEDGE® Program

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called the iPLEDGE Program.

The iPLEDGE Program is a computer-based risk management system that uses verifiable, traceable links between prescriber, patient, pharmacy, and wholesaler to control prescribing, using, dispensing, and distribution of isotretinoin.

The iPLEDGE Program is a single, shared Risk Evaluation and Mitigation Strategy (REMS) program with requirements for prescribers, pharmacies, patients, and wholesalers. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to:
- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program (see the PRECAUTIONS section of the isotretinoin Package Insert).

The traceable links of the iPLEDGE Program
Key Features of The iPLEDGE Program

The iPLEDGE Program has specific requirements for prescribers, patients, pharmacies, and wholesalers.

- The iPLEDGE Program system tracks and verifies critical program elements that control access to isotretinoin.
- Only prescribers registered with and activated in the iPLEDGE Program can prescribe isotretinoin.
- Prescribers must ensure that all patients—and specifically female patients of reproductive potential—meet the requirements to be registered in the iPLEDGE Program.
- Prescribers and patients must enter required information (i.e., pregnancy test results, 2 methods of contraception used, and confirmation of patient counseling) in the iPLEDGE Program system for patients to be qualified to receive a prescription.
- Only patients who are registered by prescribers in the iPLEDGE Program can receive isotretinoin.
- Only pharmacies registered with and activated in the iPLEDGE Program can dispense isotretinoin.
- Pharmacists must receive authorization from the iPLEDGE Program system to fill and dispense every prescription.
- Manufacturers will only ship to iPLEDGE Program–registered entities (e.g., direct vendor pharmacies, wholesalers).
- Wholesalers must register annually in the iPLEDGE Program. A registered wholesaler may distribute only FDA-approved isotretinoin product.
- Only wholesalers registered with the iPLEDGE Program can distribute isotretinoin.
- Registered wholesalers can only ship to wholesalers registered in the iPLEDGE Program with prior written consent from the manufacturer or pharmacies licensed in the US and registered and activated in the iPLEDGE Program.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE Program.
Pharmacies And The iPLEDGE® Program

The iPLEDGE Program includes specific requirements that pharmacies must follow in order to dispense isotretinoin. These include:

- Designating a Responsible Site Pharmacist
- Reviewing and abiding by the Non-Compliance Action Policy (NCAP) ([www.ipledgeprogram.com](http://www.ipledgeprogram.com))
- Following the procedures to fill and dispense prescriptions

Non-Compliance Action Policy (NCAP)

The Non-Compliance Action Policy was implemented to monitor compliance, address deviations, and institute appropriate corrective actions to improve minimization of drug exposure during pregnancy and compliance with elements to assure safe use under the iPLEDGE Program. The NCAP sets forth the principles by which Non-Compliance by iPLEDGE Program stakeholders will be evaluated. The NCAP can be found on the iPLEDGE Program web site at [www.ipledgeprogram.com](http://www.ipledgeprogram.com).

Key Information For Pharmacists

The key areas pharmacists must understand and follow include:

- The Non-Compliance Action Policy (NCAP)
- **The Responsible Site Pharmacist (RSP) must register and activate the pharmacy** in the iPLEDGE Program system. The RSP must re-activate the pharmacy in the iPLEDGE Program annually.
- Prior to obtaining authorization for the pharmacy to dispense a prescription, the prescriber and patient must enter required information into the iPLEDGE Program system.
- **The dispensing pharmacist must receive a Risk Management Authorization (RMA)** before filling and dispensing prescriptions. This authorization can be obtained by one of the following ways:
  - Pharmacies that elect to utilize electronic telecommunication verification of prescriptions for the iPLEDGE Program
  - During prescription claim processing (including cash claims) the iPLEDGE Program system automatically checks to ensure that all requirements have been met for the patient to receive isotretinoin.
• Pharmacies that do NOT elect to utilize electronic telecommunication verification of prescriptions for the iPLEDGE Program
  - The pharmacy must manually obtain a Risk Management Authorization (RMA) via the iPLEDGE Program web site or phone system to ensure that all requirements have been met for the patient to receive isotretinoin. The pharmacist should ensure the RMA number is documented.

• Upon receiving authorization, the dispensing pharmacist can fill and dispense a prescription for a maximum 30-day supply of isotretinoin.

• Upon authorization, the iPLEDGE Program system provides the RMA number to the dispensing pharmacist. The pharmacist should ensure the RMA number is documented.

• Upon authorization, the iPLEDGE Program system provides a “Do Not Dispense To Patient After” date. This date is calculated as 30 days from the office visit for male patients and females of non-reproductive potential, or 7 days from the pregnancy test date for female patients of reproductive potential. It is recommended that the pharmacist write the date on the sticker and put the sticker on the prescription bag.

• Patients who present a prescription beyond this date will not be authorized in the iPLEDGE Program system to receive isotretinoin.

• Prescriptions must be obtained no later than the “Do Not Dispense To Patient After” date, and if not obtained, then the RMA must be reversed in the iPLEDGE Program system and the product returned to inventory.

• The iPLEDGE Program system only authorizes filling and dispensing prescriptions when patients have met the qualification criteria in the system.

• Prescriptions that are more than 30 days beyond the date of the office visit (for male patients and females of non-reproductive potential) or more than 7 days beyond the pregnancy test date (for females of reproductive potential) will not be authorized by the iPLEDGE Program system.

• No automatic refills are permitted.

• Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE Program.

• Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.

• An isotretinoin Medication Guide must be given to the patient each time isotretinoin is dispensed, as required by law.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found on the iPLEDGE Program web site www.ipledgeprogram.com or by calling 1-866-495-0654.
The iPLEDGE® Program Web Site And Phone System

The pharmacist can access the iPLEDGE Program system via the program web site and automated phone system:

- Web site: www.ipledgeprogram.com
- Phone system: 1-866-495-0654

The iPLEDGE Program web site and phone system can be used for:

- Activation of the pharmacy registration
- Manual authorization to fill and dispense prescriptions (for pharmacies that do NOT utilize electronic telecommunication verification of prescriptions)
- Manual reversal of approved prescriptions (for pharmacies that do NOT utilize electronic telecommunication verification of prescriptions)
- Ordering additional copies of the Pharmacist Guide, Patient Introductory Brochure, and prescription bag stickers
- Finding a wholesaler registered in the iPLEDGE Program
- Finding a pharmacy participating in the iPLEDGE Program
- FAQs (Frequently Asked Questions) (web site only)

To log in to either the web site or the phone system, the pharmacist needs the pharmacy username and password supplied upon registration. The pharmacy’s Responsible Site Pharmacist (RSP) can supply this information.

It is important that the RSP does not forget the iPLEDGE Program username, password, and Date of Personal Significance for the pharmacy. All of these items should be communicated to other pharmacists working at the pharmacy.

(Note: Date of Personal Significance is chosen by you, and can be any date that is easy for you to remember)
Program Materials

The iPLEDGE Program provides educational materials for prescribers, pharmacists, and patients.

Additional Materials

You can order additional program materials using either the web site or the phone system as follows:

1. After logging on to the web site, there are 2 ways to order materials:
   a. Using the navigation menu on the left side of the page, select the “Order Materials” button.
   OR
   b. Using the navigation menu on the left side of the page, choose “Pharmacy Information.” In the “View Information Online” section, select “To Order Educational Materials, please click here.”

2. In the phone system, log in and select the option to “Request Program Educational Materials.” Additional bag stickers can also be ordered using this process.

To Find a Registered Wholesaler

On the web site, log in and choose “Find Wholesaler” in the left navigation. A list of registered wholesalers and distributors will be presented.
The Responsible Site Pharmacist
Each pharmacy in the iPLEDGE® Program must designate a pharmacist as the Responsible Site Pharmacist. The Responsible Site Pharmacist is the point of contact for the pharmacy and the iPLEDGE Program. The Responsible Site Pharmacist performs the following tasks:

- Registers the pharmacy with the iPLEDGE Program
- Activates the pharmacy registration initially and annually; attests to program requirements
- Trains all pharmacists and pharmacy staff who participate in the filling and dispensing of isotretinoin prescriptions and keeps a log or record of the staff who have been trained
- Ensures that all pharmacy staff using the iPLEDGE Program are aware of the pharmacy’s username, password, and Date of Personal Significance for the iPLEDGE Program system

Registration
The Responsible Site Pharmacist registers the pharmacy in the iPLEDGE Program. Only one registration is needed for each pharmacy. The NCPDP number is the username for the entire pharmacy. After the Responsible Site Pharmacist registers the pharmacy, the pharmacy will receive a system password by mail.

Activation
Before a pharmacist can fill and dispense prescriptions for isotretinoin, the Responsible Site Pharmacist must activate the pharmacy’s registration in the iPLEDGE Program system. The program activation expires annually. The Responsible Site Pharmacist, representing the pharmacy, must activate annually to continue ordering, filling, and dispensing isotretinoin. Upon logging in, the iPLEDGE Program system will automatically prompt the pharmacy that their activation will soon expire. If your pharmacy’s activation expires, and you do not intend to reactivate, you must return all unused isotretinoin immediately to the manufacturer or delegate.

The iPLEDGE Program system will report the expiration date of a pharmacy’s registration. To retrieve this information on the web site, log in and choose “My Program Status” on the left navigation; in the phone system, log in and select the option to hear “Current Program Status.” Activation requires attesting to the following statements in the iPLEDGE Program system:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I will train all pharmacists who participate in the filling and dispensing of isotretinoin prescriptions on the iPLEDGE Program requirements.
• I will comply and seek to ensure all pharmacists who participate in the filling and dispensing of isotretinoin prescriptions comply with the iPLEDGE Program requirements described in the booklet entitled Pharmacist Guide, specifically the “Key Information for Pharmacists” section including the following dispensing information:
  – Prescriptions must be obtained no later than the “Do Not Dispense To Patient After” date, and if not obtained, then the RMA must be reversed in the iPLEDGE Program system and the product returned to inventory.

• I will only obtain isotretinoin from only iPLEDGE registered wholesalers.

• I will not sell, buy, borrow, loan or otherwise transfer isotretinoin in any manner to or from another pharmacy.

• I will return to the manufacturer (or delegate) any unused product if the pharmacy is deactivated by the iPLEDGE Program or if the pharmacy chooses to not reactivate annually.

• I will not fill isotretinoin for any party other than a qualified patient.

Required Steps for Pharmacies:

1. Activating The Pharmacy In The iPLEDGE Program System

Access the iPLEDGE Program system to activate the pharmacy’s registration via the web site, www.ipledgeprogram.com, or the automated phone system, 1-866-495-0654. Both the web site and the phone system provide prompts to log in and complete the initial activation. Identification in either system requires the username (NCPDP number) and the password received upon registration.

The web site is the faster and easier way to access the system. After initial activation, a pharmacy must re-activate at least annually to remain active in the iPLEDGE Program.

The iPLEDGE Program system will display the “Activate” button on the Pharmacy home page when the activation for a pharmacy is nearing expiration. However, a pharmacy can re-activate at any time using the “Activate Pharmacy Registration” button on the left-hand navigation menu on all pages.

The system requires setting the pharmacy’s Date of Personal Significance.

• The Date of Personal Significance is a date that is easily remembered and should be a date that will be known by all the pharmacists at the pharmacy. This date will be used to verify the pharmacy’s identity if required by the iPLEDGE® Program system or if the pharmacy’s password is lost.

• The same Date of Personal Significance will be used by all pharmacists in the pharmacy when contacting the iPLEDGE Call Center. If you change the Date of Personal Significance for your pharmacy, you should communicate this change to others at your pharmacy.
**Required Steps for Pharmacies (Cont.)**

2. Preparing the pharmacy to obtain RMAs
   a) Chain pharmacy organizations
      • Contact your Corporate Office for procedures to establish connectivity to the pharmacy network.
   b) Non-chain pharmacies that elect to utilize electronic telecommunication verification for the iPLEDGE Program
      • Call the iPLEDGE Program Contact Center 1-866-495-0654.
      • Sign Terms and Conditions associated with obtaining RMAs automatically via the REMS Pharmacy Network Connectivity.
      • Process test claim(s) to verify connectivity to the Pharmacy Network (including cash claim set-up).
      • Communicate the successful completion of Terms and Conditions and successful test claim processing to the iPLEDGE Program.
   c) Non-chain pharmacies that do not elect to utilize electronic telecommunication verification for the iPLEDGE Program
      • Pharmacy must obtain RMAs via the iPLEDGE Program web site or the automated phone system.
      • No additional steps required for the pharmacy to obtain RMAs.

**Using the web site**

The Responsible Site Pharmacist:
1. Logs in by entering the pharmacy username (NCPDP number) and password.
2. Changes the pharmacy password and sets the Date of Personal Significance.
3. Selects “Activate Pharmacy Registration” from the Pharmacy home page. The system will provide prompts to complete the activation process. If the current activation for a pharmacy is nearing expiration, the Pharmacy home page will prominently display a direct link to re-activate.

**Using the automated phone system**

The Responsible Site Pharmacist:
1. At the main pharmacy menu, selects the option to log in and follows the prompts to enter the pharmacy username (NCPDP number) and password.
2. Changes the pharmacy password and sets the Date of Personal Significance.
3. At the pharmacy menu, selects the option to begin the activation process.
Training Pharmacy Staff

The Responsible Site Pharmacist is responsible for the training, and the documentation of training, of all pharmacists and staff in a registered pharmacy.

The training for all pharmacists and staff must include:

- Knowing about isotretinoin teratogenicity and the contraception and program requirements of the iPLEDGE Program
- Being able to access the iPLEDGE Program system and obtain authorization to fill and dispense a prescription
- Correctly using the RMA number and “Do Not Dispense To Patient After” date
- Familiarity with the Non-Compliance Action Policy and the sanctions that can occur for pharmacy Non-Compliance activities

Training begins by providing the Pharmacist Guide to all pharmacists. Additional copies can be requested through the iPLEDGE Program web site and the iPLEDGE Program phone system.

The Responsible Site Pharmacist should review the following sections with each pharmacist after he/she has read the material:

- Isotretinoin teratogenicity and measures to reduce fetal exposure (see “About Isotretinoin,” page 4)
- Accessing the iPLEDGE Program system via web site and phone system, using username (NCPDP number) and system password (see page 10)
- iPLEDGE Program procedures for filling and dispensing prescriptions (see page 16)
- Time limitations on dispensing (see page 16)
- Patient qualification criteria (see page 19)
- Effective primary and secondary methods of contraception (see page 21)
- Additional contraception information and counseling about pregnancy (see page 25)

After the Responsible Site Pharmacist reviews the material, he/she should:

- Review the steps with the pharmacy staff for accessing the iPLEDGE Program system and the procedures for obtaining authorization to fill a prescription
- Ensure that pharmacy staff has the Date of Personal Significance, username, and password necessary to log in to the iPLEDGE Program system
- Record the date of training, have each pharmacist and staff member sign a log or record of training, and co-sign this training record
Changing The Responsible Site Pharmacist

The pharmacy can change its designated Responsible Site Pharmacist at any time. To make the change the new Responsible Site Pharmacist or the former Responsible Site Pharmacist must call the iPLEDGE® Program at 1-866-495-0654 and select #0 to transfer to the Call Center. The new Responsible Site Pharmacist must re-activate the pharmacy in the iPLEDGE Program (for activation information, see page 12). If the pharmacy activation expires, and you do not intend to reactivate, you must return all unused isotretinoin immediately to the manufacturer or their delegate.

Procedure For Filling And Dispensing Prescriptions

Confirm patient qualification and obtain authorization by one of the following ways:

1. Pharmacies that elect to utilize electronic telecommunication verification of prescriptions for the iPLEDGE Program

   • The iPLEDGE Program system automatically checks to ensure that all requirements have been met for the patient to receive isotretinoin during prescription claim processing (cash claims must also be processed through the pharmacy management system).

   • If authorized to fill and dispense the iPLEDGE Program system provides the following:

     • RMA number—captured by the pharmacy practice management system.
     • “Do Not Dispense To Patient After” date—it is highly recommended that the pharmacist write the date on the sticker and put the sticker on the prescription bag.

   • If not authorized to fill and dispense:

     • The claim will not be approved.
     • The pharmacy claim (whether cash or third party) will continue to be rejected by the system until all criteria are met. The system will provide information regarding the reason for the rejected claim.
     • Pharmacists cannot manually override a rejected claim.
     • Pharmacy staff are not authorized to dispense any quantity of isotretinoin that the iPLEDGE Program system does not authorize.

Note: If more than one strength is required to achieve the desired dosage, an RMA must be obtained for each strength.
2. Pharmacies that do NOT elect to utilize electronic telecommunication verification of prescriptions for the iPLEDGE Program

- The pharmacy must manually obtain access to the iPLEDGE Program web site or phone system to check patient qualification criteria (current process).

The pharmacist:

- Accesses the iPLEDGE Program system via the web site, www.ipledgeprogram.com, or the automated phone system, 1-866-495-0654
- Logs in using the pharmacy username (NCPDP number) and the pharmacy password
  - On the web site, chooses “Fill Prescriptions” from the left navigation
  - In the phone system, selects the option to “Obtain Approval to Fill or Reverse a Prescription”
- Enters the patient ID number from the patient ID card
- Enters the patient’s date of birth
- Prescriptions will be authorized only for those patients who meet all criteria.
- If authorized to fill and dispense, the pharmacist enters the:
  - NDC
  - Days supply
  - Quantity dispensed
- System provides:
  - An RMA number to be documented
  - A “Do Not Dispense To Patient After” date. It is recommended that the pharmacist write the date on the sticker and put the sticker on the prescription bag.

Note: If more than one strength is required to achieve the desired dosage, an RMA must be obtained for each strength.

- The pharmacist may proceed with normal insurance adjudication only if the iPLEDGE Program system has authorized dispensing.
- The pharmacist may not proceed with normal insurance adjudication and may not dispense isotretinoin if dispensing is not authorized in the iPLEDGE Program system.
- If not authorized to fill and dispense:
  - The system will provide information or instructions for the patient (e.g., “Please contact your doctor/prescriber”)
Procedure For Filling And Dispensing Prescriptions (Cont.)

Dispense the prescription

- Only FDA-approved products may be dispensed.
- The system will automatically calculate and provide the “Do Not Dispense To Patient After” date to the pharmacist. The pharmacist must not dispense the prescription after this date.
- A maximum 30-day supply of isotretinoin may be dispensed.
- Refills are not allowed. Monthly continuation of treatment requires the patient to fulfill the iPLEDGE® Program requirements to obtain a new prescription.

IMPORTANT NOTE: Per the Non-Compliance Action Policy (NCAP), any pharmacy that receives a denial to fill the prescription in the iPLEDGE Program system, but dispenses the prescription without an RMA will be subject to a 90-day Temporary Deactivation.

Prescription bag stickers

- The bag sticker has space for the “Do Not Dispense To Patient After” date.
- It is recommended that the pharmacist write the date on the sticker and put the sticker on the prescription bag.
- Additional stickers can be ordered.

DO NOT DISPENSE ISOTRETINOIN AFTER THE “DO NOT DISPENSE TO PATIENT AFTER” DATE

Non-dispensed prescriptions

If the prescription is not dispensed for any reason (e.g., the patient did not obtain, dispense date expired, third party did not authorize payment) the authorization to dispense must be reversed in the system.

- If the RMA was obtained via electronic telecommunication, the pharmacist can reverse the electronic claim authorization and return the product to stock. The RMA will automatically be reversed in the iPLEDGE Program system upon claim reversal.
- If the RMA was obtained manually via the iPLEDGE Program web site, the pharmacist must log in to the web site and select “Reverse Prescription” in order to perform an RMA reversal and then return the product to stock.
- If the RMA was obtained manually via the iPLEDGE Program phone system, the pharmacist should call 1-866-495-0654, log in, and select the option “RMA or Reverse a Prescription,” follow the prompts to perform an RMA reversal and then return the product to stock.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
iPLEDGE Program General Information

The following section covers general aspects of the iPLEDGE Program.

All Patients

To receive isotretinoin, all patients must meet all of the following conditions:

1. **Must** be registered with the iPLEDGE Program by the prescriber
2. **Must** understand that severe birth defects can occur with the use of isotretinoin by female patients
3. **Must** be reliable in understanding and carrying out instructions
4. **Must** sign a Patient Information/Informed Consent (for all patients) form that contains warnings about the potential risks associated with isotretinoin
5. **Must** obtain the prescription within their prescription window as follows:
   - Male patients and female patients who cannot get pregnant, prescriptions must be obtained within the 30-day prescription window, counting the office visit as DAY 1.
   - Female patients who can get pregnant, prescriptions must be obtained within the 7-day prescription window, counting the day of the blood draw or urine sample as DAY 1.
6. **Must** not donate blood while on isotretinoin and for 1 month after treatment has ended
7. **Must** not share isotretinoin with anyone, even someone who has similar symptoms

All patients should understand that refills are not allowed. Patients can only receive a maximum of 30-day supply of isotretinoin per prescription. For each prescription, continuation of treatment requires the patient to satisfy the iPLEDGE Program requirements to obtain a new prescription. The prescriber must also counsel the patient each month about the iPLEDGE Program requirements and then confirm via the iPLEDGE Program automated system that this counseling occurred.
**Females of Reproductive Potential**

Once the prescriber decides to pursue qualification of the patient, a female of reproductive potential must follow these steps.

1. Females of reproductive potential must have had 2 negative urine or serum pregnancy tests with a sensitivity of at least 25 mIU/mL before receiving the initial isotretinoin prescription. The first test (a screening test) is obtained by the prescriber when the decision is made to pursue qualification of the patient for isotretinoin. There is a 30-day wait period where the patient must be on 2 methods of birth control simultaneously. The second pregnancy test (a confirmation test) must be done in a CLIA-certified laboratory. The interval between the 2 tests must be at least 19 days.
   
   - For patients with regular menstrual cycles, the second pregnancy test must be done during the first 5 days of the menstrual period immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods of contraception for 1 month.
   
   - For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods of contraception for 1 month.
   
   - The patient must be using her 2 methods of birth control for at least 30 days prior to beginning to take isotretinoin, and her second pregnancy test must occur after this 30-day period is complete.

2. The patient must sign the Patient Information/Informed Consent (for all patients) form and the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.

3. The patient must select and commit to use 2 methods of effective contraception together, at least 1 of which must be a primary method, unless continuous abstinence is chosen. Patients must use 2 methods of effective contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment.
**iPLEDGE® Program Approved Methods of Contraception**

Choose 1 Primary + 1 Secondary Birth Control Method

<table>
<thead>
<tr>
<th>Primary Method of Birth Control (Choose One)*</th>
<th>How to Use it</th>
<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks‡</th>
</tr>
</thead>
</table>
| **Hormonal Implant**                          | Placed under skin of arm by a clinician. Works for 3 years.† | >99%† | • Nothing to do or remember  
• Light or no periods  
• May decrease acne  
• No increased risk of clots | Irregular Periods |
| **Hormonal IUD**                              | Placed in uterus by clinician. Self-check monthly. Works for 5 years.† | >99%† | • Light or no periods  
• No increased risk of clots | Irregular Periods |
| **Non-Hormonal IUD**                          | Placed in uterus by a clinician. Self-check monthly. Works for 10 years.³ | >99%³ | • No hormones  
• Periods remain regular  
• Effective immediately  
• No increased risk of clots | May cause heavier periods and cramping |
| **Tubal Sterilization**                       | Surgical procedure to close the tubes between the uterus and the ovaries. | >99%² | • It is a virtually permanent method of birth control  
• Nothing to do or remember | If you want to have child later, it is very difficult to re-open the tubes |
| **Male Vasectomy**                            | Surgical procedure that closes off the tubes that carry a partner's sperm. | >99%² | • It is a virtually permanent method of birth control  
• Nothing to do or remember | If you want to have child later, it is very difficult to re-open the tubes |
| **Hormonal Shot**                             | Given every 3 months by a clinician. | >97%¹ | • Light or no periods  
• No increased risk of clots | Irregular Periods  
• May cause weight gain |
| **Vaginal Ring**                              | You place in vagina. Replace monthly. | 92%¹ | • Lighter periods  
• May decrease acne | Blood clots |
| **Hormonal Patch**                            | You place on skin. Replace weekly. | 92%¹ | • Lighter periods  
• May decrease acne | Blood clots |
| **Birth Control Pill (Combination Type)**     | Swallow at the same time daily. | 92%¹ | • Lighter periods  
• May decrease acne | Blood clots |

<table>
<thead>
<tr>
<th>Secondary Method of Birth Control (Choose One)</th>
<th>How to Use it</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Condoms (with or without spermicide)</strong></td>
<td>Partner must be willing to use each and every time you have sex.</td>
<td>• Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS</td>
<td>Allergic Reactions</td>
</tr>
<tr>
<td><strong>Cervical Cap, Diaphragm</strong> (must be used with spermicide). Vaginal Sponge</td>
<td>Place in vagina before you have sex.</td>
<td>• You are in control of its use</td>
<td>Allergic Reactions</td>
</tr>
</tbody>
</table>

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.
†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.
Requirements For Each Prescription

In addition to the requirements for all patients, the female patient of reproductive potential has additional requirements. Prior to each prescription, she must have a negative result from a urine or serum pregnancy test. A pregnancy test must be repeated, in a CLIA-certified laboratory, prior to the female patient receiving each prescription. A pregnancy test must also be obtained at the end of treatment (after the last dose) and 1 month after the last dose. Before each prescription, the iPLEDGE* Program also requires monthly counseling about contraception and behaviors associated with an increased risk of pregnancy.

In addition to their required doctor/prescriber appointments, females of reproductive potential must also report their 2 methods of birth control in the iPLEDGE Program system and answer questions about the iPLEDGE Program and pregnancy prevention.

Unacceptable methods of contraception

- Progesterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method or fertility awareness)
- Breastfeeding
- Withdrawal
- Cervical shield*

Abstinence

For this program, all females of reproductive potential must fully commit to pregnancy prevention. Isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE Program. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence, she must understand that she has committed to not engaging in sexual activity for 1 month before she starts taking isotretinoin, while she is on isotretinoin and for 1 month after she stops taking isotretinoin.

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.

A cervical shield should not be confused with a cervical cap, which is an effective secondary method of contraception.
Patient Criteria For Authorization To Fill And Dispense

This is the information that must be entered by prescribers and patients into the iPLEDGE Program system for all patients and, specifically, for females of reproductive potential. This is the information the system uses to authorize filling a prescription and to provide the RMA number and the “Do Not Dispense To Patient After” date.

All patients
Prescriber confirms that:
• The patient is registered with the iPLEDGE Program
• The patient was counseled about the iPLEDGE Program requirements

Females of reproductive potential
Prescriber:
• Confirms that the patient was counseled about the iPLEDGE Program contraception requirements
• Enters the 2 methods of contraception that the patient is using
• Enters pregnancy test results to start the 7-day prescription window, counting the date of the specimen collection as DAY 1

Patient:
• Correctly answers the questions about pregnancy prevention and the iPLEDGE Program
• Enters the 2 methods of contraception she is using

The primary method of contraception reported by both the prescriber and the patient must match.

Note: The system will automatically provide the pharmacist with the “Do Not Dispense To Patient After” date.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
Note: The following is provided to the pharmacist for information purposes only. No action is required by the pharmacist for a patient to fulfill the requirements of the iPLEDGE® Program and become qualified to obtain a prescription.

<table>
<thead>
<tr>
<th>All patients have a specific period of time in which they can obtain their prescription. This is called the “prescription window” and its start and end dates depend on the type of patient, as follows:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female patients who can get pregnant</strong></td>
</tr>
<tr>
<td>The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1. To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken.</td>
</tr>
</tbody>
</table>

After 11:59 p.m. Eastern Time on the last day of the prescription window, the prescription can no longer be picked up, and the patient must start the process over to get a new prescription window.*

*One notable exception is that females of reproductive potential who do not obtain their first month of treatment prescription in their first 7-day prescription window, must wait at least 19 days from their most recent pregnancy test until getting their new pregnancy test. This is based on the requirement that the most recent pregnancy test prior to beginning treatment must be conducted in the first 5 days of her menstrual cycle.

There are different program requirements for male patients and females of non-reproductive potential and for females of reproductive potential.
Additional Contraception Information

The iPLEDGE Program has the Prescriber Contraception Counseling Guide available. This is the professional companion piece to the patient’s Birth Control Workbook. Copies can be requested through the iPLEDGE Program system.

Counseling a Potentially Pregnant Patient

If a patient expresses concern that she may be pregnant, tell her to stop taking isotretinoin immediately and call her prescriber.

Males And Birth Defects

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin.

Studies did not show effects on sperm count, how sperm look, or how well they swim and move.

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.

Reference

NOTES:
For iPLEDGE Program Information

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
**WARNING**
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

**IMPORTANT NOTICE**
Use only isotretinoin products approved by the US Food and Drug Administration.

Obtain isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Pharmacy Registration

Please provide your pharmacy's NCPDP number and click the Lookup Info button. This will be used as your Username to identify you in the program and for you to login to the iPLEDGE Program system using the phone or internet site.

NCPDP Number

Enter or confirm your information. All fields listed below are required unless otherwise indicated.

Responsible Site Pharmacist First Name

Responsible Site Pharmacist Last Name

Responsible Site Pharmacist License

Preferred Method of Communication

Select

Phone Number

Ext. (Optional)

Email (Optional)

Fax (Optional)

☐ This pharmacy orders isotretinoin directly from one or more of the manufacturers of isotretinoin.

Can your pharmacy management system adjudicate claims?

Yes

Save and Print

Welcome [NCPDP#]
Logout
Have Questions? Call our toll-free number 1-866-495-0564

Reference ID: 4252185
Pharmacy Registration

Please provide your pharmacy's NCPDP number and click the Lookup Info button. This will be used as your Username to identify you in the program and for you to login to the PLEDGE Program system using the phone or internet site.

NCPDP Number

Lookup Info

Enter or confirm your information. All fields listed below are required unless otherwise indicated.

Responsible Site Pharmacist First Name

Responsible Site Pharmacist Last Name

Responsible Site Pharmacist License

Preferred Method of Communication
Select

Phone Number

Ext (Optional)

Email (Optional)

Fax (Optional)

☐ This pharmacy orders isotretinoin directly from one or more of the manufacturers of isotretinoin.

Can your pharmacy management system adjudicate claims?

Yes

Click the Save and Print button below. This will present a print friendly registration form for your signature. After printing and signing, return the form to the address or fax number found on the form.

Save and Print
Pharmacy Registration

Mail To
iPLEDGE - Committed to Pregnancy Prevention
PO BOX 2904
Phoenix AZ 85063-9978

Or Fax to
1-866-495-0660

Username
2031543T

Your Information:
Male Brevik
7510 East Camelback Road
Scottsdale, AZ 85251
Phone 602-810-4466 Fax
Email test@test.com
Preferred Method of Communication Email

☐ This pharmacy orders isotretinoin directly from one or more of the manufacturers of isotretinoin

RSP Signature                                      Date

Return to Home Page
The iPLEDGE Program

Guide to Isotretinoin
For Female Patients
Who Can Get Pregnant

The Importance of Avoiding Pregnancy on Isotretinoin

The tools you need to help you prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment
– Patient ID Cards and Informed Consent forms located inside back cover pocket

WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment. Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration. Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

Reference ID: 4252185
Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

CAUSES

BIRTH DEFECTS

DO NOT GET PREGNANT
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guide to Isotretinoin for Female Patients Who Can Get Pregnant</td>
<td>4</td>
</tr>
<tr>
<td>Effective Methods of Birth Control</td>
<td>7</td>
</tr>
<tr>
<td>iPledge® Program Checklist</td>
<td>12</td>
</tr>
<tr>
<td>Patient Information/Informed Consent Forms (for all patients)</td>
<td>15*</td>
</tr>
<tr>
<td>Patient Information/Informed Consent About Birth Defects</td>
<td>15*</td>
</tr>
<tr>
<td>(for female patients who can get pregnant)</td>
<td></td>
</tr>
<tr>
<td>Patient Identification Cards</td>
<td>15*</td>
</tr>
</tbody>
</table>

*Located inside back cover pocket.
What Is Isotretinoin?

Isotretinoin (eye-soh-tret-in-OH-in) is a prescription medication that treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months. Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby’s mother takes isotretinoin. You should also learn about the side effects and the precautions and warnings (see the enclosed sheet entitled Safety Information About Isotretinoin).

What Is The iPLEDGE® Program?

To avoid serious risks to unborn babies, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for isotretinoin. The iPLEDGE Program is a single, shared (includes multiple manufacturers) system with requirements for prescribers, pharmacies, and patients. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to
- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Only registered and activated prescribers can prescribe isotretinoin and only registered and activated pharmacies can dispense isotretinoin. In order to receive isotretinoin, all patients must be enrolled in the iPLEDGE Program and agree to follow the requirements.
What Do All Patients Need To Know?

Prevent Pregnancy and Birth Defects
   There is a very high chance that babies born to female patients taking isotretinoin will be deformed, born too early, or die before they are born. This can happen even if a female patient takes isotretinoin for only a short time. It may also happen if a pregnant female receives a blood transfusion from someone taking isotretinoin.

Do male patients taking isotretinoin need to worry about birth defects?
   Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin.

   If you are worried about isotretinoin birth defects from sperm, you can use a male latex condom to help prevent pregnancy. Use a condom each and every time you have intercourse (sex) while you are taking isotretinoin and for 1 month after you stop taking it.

Can isotretinoin affect a male patient’s ability to father healthy children?
   Studies on isotretinoin did not show effects on sperm count, how sperm look, or how well they swim and move.

Do Not Donate Blood
   Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant female gets blood from you. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone
   You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

Obtain Your Prescription
   Obtain your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

   The web site, www.ipledgeprogram.com, has a list of registered pharmacies. Once on the web site choose “Find a Participating Pharmacy” in the left navigation. A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.
What Do Female Patients Who Can Get Pregnant Need To Know?

DO NOT take isotretinoin if you are pregnant.
DO NOT get pregnant before starting isotretinoin, while taking it, and for 1 month after your last dose.

Before you can begin isotretinoin treatment, there is a 30-day wait period where you must be on 2 methods of birth control. Additionally, you need to have 2 negative pregnancy tests. They can be urine or blood tests. You will need to plan with your doctor/prescriber when and where to take your pregnancy tests.

- You take the first test when you decide to take isotretinoin.
- You take the second test during the first 5 days of the menstrual period right before you start isotretinoin. This pregnancy test must be done by an approved lab. The interval between the 2 tests must be at least 19 days.

You must take a pregnancy test every month done by an approved lab during treatment. You also take a pregnancy test after your last dose, and 1 month after your last dose. You will need to plan with your doctor/prescriber when to take your pregnancy test each month.

Have 2 negative pregnancy tests before you start isotretinoin.

Have a negative pregnancy test before you obtain each monthly prescription.

To keep from getting pregnant, you need to use 2 effective methods of birth control together correctly all the time:

- For at least 1 month before you start isotretinoin
- During treatment which usually lasts 4 to 5 months
- For 1 month after your last dose—to continue protection against pregnancy

Any method of birth control can fail. Using 2 methods of birth control together all the time drastically reduces the chance that you will get pregnant.
# iPLEDGE® Program Approved Methods of Contraception

## Choose 1 Primary + 1 Secondary Birth Control Method

<table>
<thead>
<tr>
<th>Primary Method of Birth Control (Choose One)*</th>
<th>How to Use it</th>
<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks†</th>
</tr>
</thead>
</table>
| Hormonal Implant                              | Placed under skin of arm by a clinician. Works for 3 years.¹ | >99%¹ | • Nothing to do or remember  
• Light or no periods  
• May decrease acne  
• No increased risk of clots | Irregular Periods |
| Hormonal IUD                                 | Placed in uterus by clinician. Self-check monthly. Works for 5 years.¹ | >99%¹ | • Light or no periods  
• No increased risk of clots | Irregular Periods |
| Non-Hormonal IUD                             | Placed in uterus by a clinician. Self-check monthly. Works for 10 years.³ | >99%¹ | • No hormones  
• Periods remain regular  
• Effective immediately  
• No increased risk of clots | May cause heavier periods and cramping |
| Tubal Sterilization                          | Surgical procedure to close the tubes between the uterus and the ovaries. | >99%² | • It is a virtually permanent method of birth control  
• Nothing to do or remember | If you want to have child later, it is very difficult to re-open the tubes |
| Male Vasectomy                               | Surgical procedure that closes off the tubes that carry a partner’s sperm. | >99%³ | • It is a virtually permanent method of birth control  
• Nothing to do or remember | If you want to have child later, it is very difficult to re-open the tubes |
| Hormonal Shot                                | Given every 3 months by a clinician. | >97%¹ | • Light or no periods  
• No increased risk of clots | Irregular Periods  
• May cause weight gain |
| Vaginal Ring                                 | You place in vagina. Replace monthly. | 92%¹ | • Lighter periods  
• May decrease acne | Blood clots |
| Hormonal Patch                               | You place on skin. Replace weekly. | 92%¹ | • Lighter periods  
• May decrease acne | Blood clots |
| Birth Control Pill (Combination Type)        | Swallow at the same time daily. | 92%¹ | • Lighter periods  
• May decrease acne | Blood clots |

<table>
<thead>
<tr>
<th>Secondary Method of Birth Control (Choose One)</th>
<th>How to Use it</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condoms (with or without spermicide)</td>
<td>Partner must be willing to use each and every time you have sex.</td>
<td>• Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS</td>
<td>Allergic Reactions</td>
</tr>
<tr>
<td>Cervical Cap, Diaphragm (must be used with spermicide). Vaginal Sponge</td>
<td>Place in vagina before you have sex.</td>
<td>• You are in control of its use</td>
<td>Allergic Reactions</td>
</tr>
</tbody>
</table>

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.  
†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.  
Reasons you would not have to use 2 methods of birth control

There are 2 reasons you would not have to use 2 effective methods of birth control.

- You commit to abstinence which means not having sex or sexual contact with any male 24 hours a day, 7 days a week for 1 month before, during, and for 1 month after your isotretinoin treatment.

- You are unable to get pregnant because:
  - You have entered menopause, and your doctor/prescriber has confirmed this
  - You do not have either of your 2 ovaries and/or a uterus, and your doctor/prescriber has confirmed this

If you have any questions about being able to get pregnant, talk with your doctor/prescriber.

You can only obtain your prescription for isotretinoin if:

- Your pregnancy test was negative

- Your doctor/prescriber entered your 2 methods of birth control in the iPLEDGE® Program system

- You answered your comprehension questions in the iPLEDGE Program system correctly. These questions will demonstrate your understanding of the iPLEDGE Program requirements, the birth control that you have chosen, and the risks associated with isotretinoin. **Note: you can answer your comprehension questions only after your doctor/prescriber has entered your pregnancy test result and confirmed your monthly office visit in the iPLEDGE Program system.** You will need your patient ID number to answer your comprehension questions on the iPLEDGE Program web site or by calling **1-866-495-0654**

- You also entered your 2 methods of birth control and they match the birth control options entered by your doctor/prescriber

Please read the iPLEDGE Program Birth Control Information Sheet and for additional information on birth control options read the enclosed Birth Control Workbook.
The iPLEDGE Program Pregnancy Registry

Because isotretinoin causes such severe birth defects, it is very important for us to know about all the pregnancies that happen during treatment and within 1 month after the last dose. If you think you are pregnant call your doctor/prescriber. The confidential iPLEDGE Program Pregnancy Registry is a way to collect that information. It may help us prevent more pregnancies in the future.

Your doctor/prescriber will tell you about the confidential iPLEDGE Program Pregnancy Registry. You are encouraged to contact the iPLEDGE Program Pregnancy Registry at 1-800-681-7247 if you get pregnant.

Obtaining Your Prescription

You obtain the prescription within the 7-day prescription window (1 week) of the date of your pregnancy test, counting the date of the pregnancy test as DAY 1.

The iPLEDGE Program system will automatically compute the “Do Not Dispense To Patient After” date for your pharmacist.

To figure out the last date you can obtain your prescription, add 6 to the date of your pregnancy test. For example:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2 – Day 6</th>
<th>Day 7 – Last day to obtain prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of the pregnancy test</td>
<td>(Saturday, March 2 thru</td>
<td>(Thursday, March 7)</td>
</tr>
<tr>
<td>(Friday, March 1)</td>
<td>Wednesday, March 6)</td>
<td></td>
</tr>
</tbody>
</table>

The 7-day prescription window expires at 11:59 p.m. Eastern Time on Day 7 of the prescription window. Your pharmacist will not be able to fill your prescription after this time. If your 7-day prescription window expires before you obtain your prescription, you can start a new 7-day prescription window right away (unless it is your first prescription window), but you must repeat the program requirements to get another prescription. Additional information regarding the specific dates of your 7-day prescription window, and other information about your current status can be found by selecting “My Program Status” on the web site from the Patient home page (after you log in).

Note: Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.
Talk With an Expert

If you want to talk to a birth control expert, such as a gynecologist or family doctor/prescriber, about your birth control, the doctor/prescriber who prescribes isotretinoin for you can refer you. The makers of isotretinoin will pay for this referred visit. Take the Contraception Counseling Guide And Contraception Referral Form with you.

Changing Your Birth Control

Tell the doctor/prescriber who prescribes your isotretinoin if you need to change your birth control during your isotretinoin treatment. Depending on the type of birth control you change to, you may have to stop isotretinoin and wait until you have been on the new birth control for at least 1 month and have a negative pregnancy test.

Changing From Abstinence

If you have chosen abstinence (not having sex or sexual contact with any male) and you decide to start having sexual activity, you must tell the doctor/prescriber who prescribes your isotretinoin before you engage in sexual activity. Before you continue isotretinoin, you and your doctor/prescriber must make a plan to start your birth control and be sure you are not pregnant.

One of the most common reasons that women get pregnant is that they do not avoid sexual activity when they plan to be abstinent.

Video: Be Prepared, Be Protected, and Be Aware: The Risk Of Pregnancy While On Isotretinoin

Your doctor/prescriber has a video that shows the kinds of birth defects that may happen if a woman takes any amount of isotretinoin while she is pregnant. It also reviews the steps for preventing pregnancy.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Changing to a New Doctor/Prescriber

You can change your doctor/prescriber through the iPLEDGE Program web site, www.ipledgeprogram.com, by choosing “Change Primary Prescriber” from the menu or by calling 1-866-495-0654. Once you make the change, you will not be able to get any more prescriptions from your original doctor/prescriber.

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.
### BEFORE TREATMENT

**PLANNING**
- **Talk** with your doctor/prescriber about isotretinoin and the iPLEDGE Program
- **Sign** the Patient Information/Informed Consent (for all patients) form
- **Sign** the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
- **Have** your first urine or blood pregnancy test, which can be performed at the doctor’s/prescriber’s office
- **Registration**—ensure your doctor/prescriber registers you in the iPLEDGE Program. You must be registered for at least 30 days prior to your first prescription.
- **Get** your patient ID card containing your patient ID number from your doctor/prescriber. Keep your patient ID number in a safe place.
- **Receive** your password in the mail

**BIRTH CONTROL**
- **Read** the iPLEDGE Program Birth Control Information Sheet and for additional information on birth control options read the *Birth Control Workbook*
- **Talk** with your dermatologist, gynecologist, family doctor, or a birth control expert about effective birth control options
- **Choose** 2 effective methods of birth control
- **Start** using the 2 methods of birth control together for at least 1 month before you start isotretinoin

**YOUR FIRST PRESCRIPTION**
- **Have** a second pregnancy test conducted at an approved lab within the first 5 days of your menstrual period (at least 30 days after registration)
- **Answer** questions about the iPLEDGE Program and confirm your 2 methods of birth control
  - **Note:** you can answer your comprehension questions only after your doctor/prescriber has entered your pregnancy test result in the iPLEDGE Program system
- **Obtain** your prescription for up to a maximum of a 30-day supply
  - **Note:** isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack and provide fewer than 10 capsules.
- **Obtain** your prescription within the 7-day prescription window, counting the date of the pregnancy test as DAY 1
  - **If you do not obtain your prescription within the 7-day prescription window, you will need to go back to your doctor/prescriber to start this process again**
- **Use 2 effective methods of birth control together all the time**
- **Keep** your appointments every month to get a prescription
- **See** your doctor/prescriber for a monthly pregnancy test
- **Answer** different questions each month about the iPLEDGE Program

### DURING TREATMENT

- **Use 2 effective methods of birth control together all the time**
- **See** your doctor/prescriber for a monthly pregnancy test
- **Keep** your appointments every month to get a prescription
- **Confirm** your 2 methods of birth control by entering them into the iPLEDGE Program system
- **Answer** different questions each month about the iPLEDGE Program
- **Obtain** your prescription for up to a maximum of a 30-day supply
  - **If you do not obtain your prescription within the 7-day prescription window, you will need to go back to your doctor/prescriber to start this process again**
- **Do not donate** blood

### AFTER TREATMENT

**RIGHT AFTER YOUR LAST DOSE**
- **Get** a pregnancy test after your last dose
- **Confirm** that your doctor/prescriber has entered the results of this pregnancy test into the iPLEDGE Program system
- **Continue** using your 2 methods of birth control for 1 month
- **Do not share any leftover isotretinoin with anyone**
- **Do not donate** blood for 1 month after your last dose

**ONE MONTH AFTER YOUR LAST DOSE**
- **Have** a final pregnancy test at 1 month after your last dose
- **Confirm** that your doctor/prescriber has entered the results of this pregnancy test into the iPLEDGE Program system

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Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Reference ID: 4252185

Web site: [www.ipledgeprogram.com](http://www.ipledgeprogram.com)
Phone system: 1-866-495-0654
Patient Information/Informed Consent
Informed Consent About Birth Defects

Important forms you must sign before you begin taking isotretinoin.

Patient Identification Cards

Remove one ID card and take it along with your prescription to the pharmacy (within your prescription window) to obtain your isotretinoin. Separate the cards and keep the duplicate ID card in a safe place.
Patient Information/Informed Consent (for all patients):

To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.

Read each item below and initial in the space provided if you understand each item and must also read and understand each item before signing the agreement.

Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I, ___________________________ (Patient’s Name)
   understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.
   Initials: ______

2. My doctor has told me about my choices for treating my acne.
   Initials: ______

3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. [Note: There is a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)].
   Initials: ______

4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, “anxious” or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives. There were reports that some of these people did not appear depressed. There have been reports of patients on isotretinoin becoming aggressive or violent. No one knows if isotretinoin caused these behaviors or if they would have happened even if the person did not take isotretinoin. Some people have had other signs of depression while taking isotretinoin (see #7).
   Initials: ______

5. Before I start taking isotretinoin, I agree to tell my doctor if I have ever had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.
   Initials: ______

I now allow my doctor ___________________________ to begin my treatment with isotretinoin.

Patient Signature: ___________________________ Date: ___________________________

Parent/Guardian Signature (if under age 18): ___________________________ Date: ___________________________

Patient Address: __________________________________________________________ Telephone: __________ __________

I have:
• fully explained to the patient, ___________________________, the nature and purpose of isotretinoin treatment, including its benefits and risks
• provided the patient the appropriate educational materials, such as the Patient Introductory Brochure and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin
• answered those questions to the best of my ability

Doctor Signature: ___________________________ Date: ___________________________

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT’S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.
Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)

To be completed by the patient (and her parent or guardian* if patient is under age 18) and signed by her doctor.

Read each item below and initial in the space provided to show that you understand each item and agree to follow your doctor’s instructions. Do not sign this consent and do not take isotretinoin if there is anything that you do not understand.

* A parent or guardian of a minor patient (under age 18) must also read and initial each item before signing the consent.

(Patient’s Name)

1. I understand that there is a very high chance that my unborn baby could have severe birth defects if I am pregnant or become pregnant while taking isotretinoin. This can happen with any amount and even if taken for short periods of time. This is why I must not be pregnant while taking isotretinoin.

Initial: ______

2. I understand that I must not get pregnant one month before, during the entire time of my treatment, and for one month after the end of my treatment with isotretinoin.

Initial: ______

3. I understand that I must avoid sexual intercourse completely, or I must use two separate, effective methods of birth control (contraception) at the same time. The only exceptions are if I have had surgery to remove the uterus (a hysterectomy) or both of my ovaries (bilateral oophorectomy), or my doctor has medically confirmed that I am post-menopausal.

Initial: ______

4. I understand that hormonal birth control products are among the most effective methods of birth control. Combination birth control pills and other hormonal products include skin patches, shots, under-the-skin implants, vaginal rings, and intrauterine devices (IUDs). Any method of birth control can fail. That is why I must use two different birth control methods at the same time, starting one month before, during, and for one month after stopping therapy every time I have sexual intercourse, even if one of the methods I choose is hormonal birth control.

Initial: ______

5. I understand that the following are effective methods of birth control:

- **Primary methods**
  - tying my tubes (tubal sterilization)
  - male vasectomy
  - intrauterine device
  - hormonal (combination birth control pills, skin patches, shots, under-the-skin implants, or vaginal ring)

- **Secondary methods**
  - male latex condom with or without spermicide
  - diaphragm with spermicide
  - cervical cap with spermicide
  - vaginal sponge (contains spermicide)

A diaphragm and cervical cap must each be used with spermicide, a special cream that kills sperm.

I understand that at least one of my two methods of birth control must be a primary method.

Initial: ______

6. I will talk with my doctor about any medicines including herbal products I plan to take during my isotretinoin treatment because hormonal birth control methods may not work if I am taking certain medicines or herbal products.

Initial: ______

7. I may receive a free birth control counseling session from a doctor or other family planning expert. My isotretinoin doctor can give me an Isotretinoin Contraception Referral Form for this free consultation.

Initial: ______

My doctor has answered all my questions about isotretinoin and I understand that it is my responsibility not to get pregnant one month before, during isotretinoin treatment, or for one month after I stop taking isotretinoin.

Initial: ______

I now authorize my doctor ____________________________ to begin my treatment with isotretinoin.

Patient Signature: ____________________________ Date: __________

Parent/Guardian Signature (if under age 18): ____________________________ Date: __________

Please print: Patient Name and Address ____________________________ Telephone ____________________________

I have fully explained to the patient, ____________________________ the nature and purpose of the treatment described above and the risks to females of reproductive potential. I have asked the patient if she has any questions regarding her treatment with isotretinoin and have answered those questions to the best of my ability.

Doctor Signature: ____________________________ Date: __________
Visit your doctor/prescriber monthly
Women who can get pregnant must:
1. Have a monthly pregnancy test
2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
Do not get pregnant
Do not share your drug
Do not donate blood

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

Reference ID: 4252185
WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.
Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Visit your doctor monthly
Women who can get pregnant must:
1. Have a monthly pregnancy test
2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
Do not get pregnant
Do not share your drug
Do not donate blood

Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
Do not get pregnant
Do not share your drug
Do not donate blood

Stop isotretinoin and call your doctor right away if you are pregnant.
Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating

- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

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WARNING
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
# TABLE OF CONTENTS

- Contraception counseling for isotretinoin patients ........................................ 3
- Counseling goals .................................................................................................. 6
- Contraception requirements ................................................................................ 7
- Unacceptable methods of contraception ............................................................... 9
- Emergency contraception .................................................................................... 9
- Abstinence ............................................................................................................. 9
- Reporting a pregnancy .......................................................................................... 10
- Contraception referral form .................................................................................. 11*
- Reimbursement referral form .................................................................................. 11*

*Located inside back cover pocket.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Contraception Counseling For Isotretinoin Patients

Isotretinoin is used to treat severe recalcitrant nodular acne; however, it is also a known human teratogen. Over one third of all babies exposed to isotretinoin in utero and carried to term have major birth defects.\textsuperscript{1,2}

What Is The iPLEDGE® Program?

To avoid serious risks to unborn babies, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for isotretinoin. The iPLEDGE Program is a single, shared (includes multiple manufacturers) system with requirements for prescribers, pharmacies, and patients. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to

- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Only registered and activated prescribers can prescribe isotretinoin and only registered and activated pharmacies can dispense isotretinoin. In order to receive isotretinoin, all patients must be enrolled in the iPLEDGE Program and agree to follow the requirements.
Your Role

This patient is being referred to you because she has asked for counseling to help her decide which contraceptive methods are best for her and that will enable her to comply with the contraception requirements of the iPLEDGE® Program.

The patient must select and commit to using 2 methods of effective contraception simultaneously, at least 1 of which must be a primary method, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. She must use 2 methods of effective contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment.

**Isotretinoin is not recommended for sexually active females of reproductive potential whom you believe will not be able to maintain abstinence or will not use contraception, as the program requires.**

Please read this *Contraception Counseling Guide And Contraception Referral Form* completely before you begin your counseling session. These provide an overview of the counseling goals for the patient and the contraception requirements of the iPLEDGE Program. They do not contain detailed information on the various methods of contraception.

The *Birth Control Workbook*, which is for patients, contains more information on effective primary and secondary methods of contraception. It is not complete information on any of the methods, and the patient is encouraged to ask questions about specific methods or issues. Additionally, the patient received an iPLEDGE Program Birth Control Information Sheet which lists the approved primary and secondary methods of birth control required for the iPLEDGE Program ([www.ipledgeprogram.com](http://www.ipledgeprogram.com)).
### Primary Method of Birth Control (Choose One)*

<table>
<thead>
<tr>
<th>Method</th>
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<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks†</th>
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<tbody>
<tr>
<td><strong>Hormonal Implant</strong></td>
<td>Placed under skin of arm by a clinician. Works for 3 years.¹</td>
<td>&gt;99%¹</td>
<td>• Nothing to do or remember&lt;br&gt;• Light or no periods&lt;br&gt;• May decrease acne&lt;br&gt;• No increased risk of clots</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td><strong>Hormonal IUD</strong></td>
<td>Placed in uterus by clinician. Self-check monthly. Works for 5 years.¹</td>
<td>&gt;99%¹</td>
<td>• Light or no periods&lt;br&gt;• No increased risk of clots</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td><strong>Non-Hormonal IUD</strong></td>
<td>Placed in uterus by a clinician. Self-check monthly. Works for 10 years.³</td>
<td>&gt;99%³</td>
<td>• No hormones&lt;br&gt;• Periods remain regular&lt;br&gt;• Effective immediately&lt;br&gt;• No increased risk of clots</td>
<td>May cause heavier periods and cramping</td>
</tr>
<tr>
<td><strong>Tubal Sterilization</strong></td>
<td>Surgical procedure to close the tubes between the uterus and the ovaries.</td>
<td>&gt;99%²</td>
<td>• It is a virtually permanent method of birth control&lt;br&gt;• Nothing to do or remember</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
</tr>
<tr>
<td><strong>Male Vasectomy</strong></td>
<td>Surgical procedure that closes off the tubes that carry a partner's sperm.</td>
<td>&gt;99%²</td>
<td>• It is a virtually permanent method of birth control&lt;br&gt;• Nothing to do or remember</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
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<td><strong>Hormonal Shot</strong></td>
<td>Given every 3 months by a clinician.</td>
<td>&gt;97%¹</td>
<td>• Light or no periods&lt;br&gt;• No increased risk of clots</td>
<td>Irregular Periods&lt;br&gt;• May cause weight gain</td>
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<tr>
<td><strong>Vaginal Ring</strong></td>
<td>You place in vagina. Replace monthly.</td>
<td>92%¹</td>
<td>• Lighter periods&lt;br&gt;• May decrease acne</td>
<td>Blood clots</td>
</tr>
<tr>
<td><strong>Hormonal Patch</strong></td>
<td>You place on skin. Replace weekly.</td>
<td>92%¹</td>
<td>• Lighter periods&lt;br&gt;• May decrease acne</td>
<td>Blood clots</td>
</tr>
<tr>
<td><strong>Birth Control Pill</strong></td>
<td>Swallow at the same time daily.</td>
<td>92%¹</td>
<td>• Lighter periods&lt;br&gt;• May decrease acne</td>
<td>Blood clots</td>
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### Secondary Method of Birth Control (Choose One)

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<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Condoms</strong> (with or without spermicide)</td>
<td>Partner must be willing to use each and every time you have sex.</td>
<td>Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS</td>
<td>Allergic Reactions</td>
</tr>
<tr>
<td><strong>Cervical Cap, Diaphragm</strong> (must be used with spermicide). <strong>Vaginal Sponge</strong></td>
<td>Place in vagina before you have sex.</td>
<td>You are in control of its use</td>
<td>Allergic Reactions</td>
</tr>
</tbody>
</table>

---

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.

†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.


Counseling Goals

Ensure That The Patient:

- Understands and commits fully to not becoming pregnant
- Commits to using 2 methods of contraception together simultaneously, consistently, and correctly. She must use 2 methods of effective contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment
- Chooses the methods of contraception that will work best for her and that she and her partner will actually use
- If, after counseling, the patient recognizes she will not be able to commit fully to the iPLEDGE® Program contraception requirements, encourage her to not take isotretinoin and do not prescribe or if counseling, inform her prescriber
- Commits fully to abstinence (not having sex or sexual contact with any male 24 hours a day, 7 days a week) for 1 month before, during, and for 1 month after she stops taking isotretinoin
- Knows when to contact her prescriber for emergency contraception
- Understands the risk of having a child with significant birth defects from exposure to isotretinoin

Counseling Younger Teens

For younger teens, it is important to stress the following aspects of contraception for the iPLEDGE Program during counseling:

- Why it is important to use 2 methods of birth control, 1 primary and 1 secondary at all times. Younger teens may need more emphasis on this point to fully understand it and comply.
- Emergency contraception. Younger teens may need more explanation from you about the need to take immediate action if they have unprotected sex or if their contraception method fails.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Contraception Requirements

Using 2 Methods of Contraception Provides More Protection

Use of 2 iPLEDGE Program approved methods of contraception (at least 1 of which is a primary method) simultaneously substantially reduces the risk that a female will become pregnant.

In addition, it is not known if hormonal contraceptives are less effective when used with isotretinoin. Because of this possibility and the fact that all contraceptive methods are less than 100% effective, the iPLEDGE Program requires the additional protection of a second method of contraception.

Selecting an Effective Primary Method of Contraception

Table 1 lists, by typical use failure rate, the primary methods of contraception acceptable in the iPLEDGE Program. The single most important decision in contraception for the iPLEDGE Program is selecting a primary method that the patient can and will use as correctly as possible. Other important factors to consider in counseling the patient on selecting a primary method include side effects, contraindications, and the patient’s ability to use it correctly. All of these factors influence compliance with the iPLEDGE Program requirements to prevent pregnancy.

Hormonal Combination Oral Contraceptives as a Primary Method

If the patient is currently taking or planning to take oral contraceptives, review that section in the Birth Control Workbook with her. For a patient who has indicated she has difficulty taking oral contraceptives correctly, other contraception not requiring daily dosing may be a better choice. It is critical that such a patient choose a method other than daily oral contraceptive agents.
Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

<table>
<thead>
<tr>
<th>Method</th>
<th>Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implanted Hormones</td>
<td>0.05%</td>
</tr>
<tr>
<td>Male Vasectomy</td>
<td>0.10%</td>
</tr>
<tr>
<td>Hormonal IUD (LNg 20)</td>
<td>0.20%</td>
</tr>
<tr>
<td>Tubal Sterilization</td>
<td>0.50%</td>
</tr>
<tr>
<td>Non-hormonal IUD (Copper T380A)</td>
<td>0.80%</td>
</tr>
<tr>
<td>Hormonal Injectable (single)</td>
<td>0.20%</td>
</tr>
<tr>
<td>Hormonal Transdermal Patch</td>
<td>0.30%</td>
</tr>
<tr>
<td>Hormonal Vaginal Ring</td>
<td>0.30%</td>
</tr>
<tr>
<td>Hormonal Combination Oral Contraceptives</td>
<td>0.30%</td>
</tr>
</tbody>
</table>

Table 1: Primary Methods of Contraception by Typical Use Failure Rate

Selecting an Effective Secondary Method of Contraception

Table 2 lists the acceptable secondary methods of contraception in the iPLEDGE® Program. There are 2 methods of secondary contraception: barrier and other. Barrier methods include the diaphragm and cervical cap (both of which must be used with a spermicide) and the male latex condom (which can be used with or without a spermicide). The other method is the vaginal sponge, which contains a spermicide. The most important issue for a secondary method is that it be used correctly each time the patient has intercourse and that it be in place should the primary method fail.

Help the patient select a secondary method that she and her partner can fully commit to using correctly each time they have intercourse.

<table>
<thead>
<tr>
<th>Method</th>
<th>Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Latex Condom</td>
<td>2%</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>6%</td>
</tr>
<tr>
<td>Cervical Cap</td>
<td>9%</td>
</tr>
<tr>
<td>Vaginal Sponge</td>
<td>9%</td>
</tr>
</tbody>
</table>

Table 2: Secondary Methods of Contraception Listed by Typical Use Failure Rate

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b. The IUD Progesterone T and progestin-only “mini-pills” are not acceptable for the iPLEDGE® Program. (See “Unacceptable Methods Of Contraception” on page 9.)

c. Failure rate for nulliparous women. The rate is approximately double for parous women.

*Failure rates for diaphragm and cervical cap are for methods including the use of spermicide.
Unacceptable Methods of Contraception

The following methods of contraception are not acceptable for the iPLEDGE Program:

- Progesterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method or fertility awareness)
- Breastfeeding
- Withdrawal
- Cervical shield, a silicone disc with a one-way air valve that creates suction to adhere to the cervix*

Patients currently using these unacceptable methods of contraception must switch to iPLEDGE Program approved methods of contraception.

Emergency Contraception

Review this section in the Birth Control Workbook with the patient. She should know when to call her prescriber for possible emergency contraception. She should also realize that emergency contraception should not be used on a regular basis as a replacement for the other contraceptive methods she selected.

Abstinence

For this program, all females of reproductive potential must fully commit to pregnancy prevention.

Isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE Program. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence, she must understand that she has committed to not engaging in sex or sexual contact with any male 24 hours a day, 7 days a week for 1 month before, during, and for 1 month after she stops taking isotretinoin.

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.

*A cervical shield should not be confused with a cervical cap, which is an effective secondary method of contraception.
About The Referral Form

The Isotretinoin Contraception Referral form, brought in to you by this patient, has been filled out in part by the prescriber. Please fill out the rest of the form at the conclusion of your counseling session and fax or mail the copy back to the prescriber, keeping a copy for your own records.

Reimbursement Form

Also in the back pocket is a reimbursement form for contraceptive counseling services. The iPLEDGE® Program provides reimbursement for 1 contraception counseling session for patients who have been prescribed isotretinoin. Please complete the form and fax it to 1-866-495-0660.

Reporting a Pregnancy

If you become aware of a pregnancy in a patient taking isotretinoin, please report the pregnancy to the iPLEDGE Program by calling 1-866-495-0654 and choosing the option to “Report a Pregnancy.”

Please remind any patient who is pregnant to contact the doctor/prescriber who prescribed her isotretinoin.

REFERENCES


Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
ISOTRETINOIN CONTRACEPTION REFERRAL FORM
Prescriber: Complete for Patients Being Referred for Contraception Counseling

Patient______________________________________, iPLEDGE Program ID#__________________________
is considering treatment with isotretinoin. I am referring her for counseling to help her choose her 2 methods
of contraception before she receives her first prescription.

Please complete the Record of Contraception Counseling below and return this form to my office, via fax or mail.
She had a negative (serum/urine) pregnancy test on__________________________

Please review this Contraception Counseling Guide for details on the iPLEDGE Program contraception requirements.

Isotretinoin Prescriber's Name__________________________________________________________
Address____________________________________________________________________________
Telephone________________________ Fax________________________
Isotretinoin Prescriber's Signature____________________________________________________
Date________________________

RECORD OF CONTRACEPTION COUNSELING
Contraception Counselor: Complete Form and Fax or Mail Back to Isotretinoin Prescriber

I have provided the following for your patient__________________________________________
    ☐ Comprehensive contraception counseling
    ☐ Information about emergency contraception

The patient has:
    ☐ Chosen 2 methods of contraception
    ☐ Committed to abstain from any sexual contact with a male and is not planning to use 2 methods of
    contraception. I informed her that abstinence without using contraception is not recommended
    for the iPLEDGE Program for sexually active women.
    ☐ Not yet decided upon the methods of contraception she will use

Primary Method________________________________________________________
Secondary or Second Primary Method________________________________________

I have prescribed the selected contraception.
    ☐ Yes ☐ No (Please comment below)

I believe that this patient is fully committed to complying with the contraceptive requirements of the
iPLEDGE Program.
    ☐ Yes ☐ No (Please comment below)

________________________________________________________
Name________________________________________________________
Address_______________________________________________________________________
Telephone________________________
Specialty (circle one): OB-GYN  Fam Prac  IM  RN  LPN  Other_______________________
Contraception Counselor's Signature___________________________________________
Date________________________

Prescriber Copy-White  Contraception Counselor Copy-Yellow  Patient Copy-Pink
FAXABLE REIMBURSEMENT FORM
The Following Restrictions Apply:
Only consulting clinicians who provide initial pregnancy prevention counseling are eligible for reimbursement for such counseling. Other services provided during this visit are not eligible for reimbursement. The physician prescribing isotretinoin, or any other person working under the direct supervision of said physician, is not eligible for this reimbursement provision. The reimbursement fee is up to $150.00, which has been determined to be an average, usual, and customary reimbursement for service of this type. Information will be used only for reimbursement; the isotretinoin manufacturers will not use it for any other purpose.

Reimbursement For Pregnancy Prevention Counseling
To receive reimbursement for providing pregnancy prevention counseling to an isotretinoin patient, please answer the following questions, and sign, date, and send the completed form via fax to 1-866-495-0660.

Contraception Counselor Name ____________________________
Payee Name (if different than Contraceptive Counselor) ____________________________
Office Telephone Number ___________________ Tax ID Number ___________________
Payee Address ____________________________________________ State ______ ZIP _______
City ____________________________
Name of Referring Physician ____________________________
Office Telephone Number ____________________________
City ____________________________ State ______ ZIP _______

Patient’s Name _________________________________________
Patient’s iPLEDGE Program ID Number _________________________

☐ I have provided pregnancy prevention counseling to this patient. I have mailed or faxed the record of pregnancy prevention counseling (on reverse side) to the isotretinoin prescriber.
☐ I am not the prescribing physician of isotretinoin to the patient referenced above, nor am I employed by said prescribing physician.
☐ I have not, and will not, bill or submit for reimbursement either directly or indirectly, under Medicaid, Medicare, or similar federal or state healthcare programs, or under any private insurance, HMO, or other healthcare benefit program for the pregnancy prevention counseling services described above.
☐ I attest that all of the above information is accurate and understand that I must check each box above to receive reimbursement.
☐ I have included a signed W-9 Form, or already have a W-9 form on file for payment from iPLEDGE. A blank W-9 form and instructions for completion can be found at www.irs.gov

Signature ____________________________ Date _____________
FAXABLE REIMBURSEMENT FORM

The Following Restrictions Apply:

Only consulting clinicians who provide initial pregnancy prevention counseling are eligible for reimbursement for such counseling. Other services provided during this visit are not eligible for reimbursement. The physician prescribing isotretinoin, or any other person working under the direct supervision of said physician, is not eligible for this reimbursement provision. The reimbursement fee is up to $150.00, which has been determined to be an average, usual, and customary reimbursement for service of this type. Information will be used only for reimbursement; the isotretinoin manufacturers will not use it for any other purpose.

Reimbursement For Pregnancy Prevention Counseling
**WARNING**
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

**IMPORTANT NOTICE**
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
The iPLEDGE Program

Isotretinoin Educational Kit for Male Patients and Female Patients Who Cannot Get Pregnant

The tools you need to help you prepare and plan treatments during the course of isotretinoin treatment

WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.

Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
CAUSES

BIRTH DEFECTS

DO NOT GET PREGNANT
TABLE OF CONTENTS

Guide for Male Patients and Female Patients Who Cannot Get Pregnant ........ 4

iPLEDGE® Program Checklist ........................................................................ 7

Patient Information/Informed Consent (for all patients) ......................... 11*

Safety Information About Isotretinoin ...................................................... 11*

Patient Identification Cards .................................................................... 11*

*Located inside back cover pocket.
What Is Isotretinoin?

Isotretinoin (eye-soh-tret-in-OH-in) is a prescription medication that treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months. Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby’s mother takes isotretinoin. You should also learn about the side effects and the precautions and warnings (see the enclosed sheet entitled Safety Information About Isotretinoin).

What Is The iPLEDGE® Program?

To avoid serious risks to unborn babies, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for isotretinoin. The iPLEDGE Program is a single, shared (includes multiple manufacturers) system with requirements for prescribers, pharmacies, and patients. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to
- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Only registered and activated prescribers can prescribe isotretinoin and only registered and activated pharmacies can dispense isotretinoin. In order to receive isotretinoin, all patients must be enrolled in the iPLEDGE Program and agree to follow the requirements.
What Do All Patients Need To Know?

Prevent Pregnancy and Birth Defects
There is a very high chance that babies born to female patients taking isotretinoin will be deformed, born too early, or die before they are born. This can happen even if a female patient takes isotretinoin for only a short time. It may also happen if a pregnant female receives a blood transfusion from someone taking isotretinoin.

Do male patients taking isotretinoin need to worry about birth defects?
Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin.
If you are worried about isotretinoin birth defects from sperm, you can use a male latex condom to help prevent pregnancy. Use a condom each and every time you have intercourse (sex) while you are taking isotretinoin and for 1 month after you stop taking it.

Can isotretinoin affect a male patient’s ability to father healthy children?
Studies on isotretinoin did not show effects on sperm count, how sperm look, or how well they swim and move.

Do Not Donate Blood
Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant female gets blood from you. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone
You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

Obtain Your Prescription
Obtain your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
The web site, www.ipledgeprogram.com, has a list of registered pharmacies. Once on the web site choose “Find a Participating Pharmacy” in the left navigation. A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.
What Do Male Patients And Female Patients Who Cannot Get Pregnant Need To Know?

You can only obtain isotretinoin if:

- You are registered in the iPLEDGE® Program, your doctor/prescriber has entered your patient information in the iPLEDGE Program system, and you have your patient ID number.

- You must obtain the prescription within the 30-day prescription window, counting the office visit as DAY 1. The 30-day prescription window expires at 11:59 p.m. Eastern Time on Day 30 of the prescription window.

The iPLEDGE Program system will automatically compute the “Do Not Dispense To Patient After” date for your pharmacist.

To figure out the last date you can obtain your prescription, add 29 days to the date of your office visit. For example:

Day 1 and Day of the office visit
(Friday, March 1)

Day 2 – Day 29
(Saturday, March 2 thru Friday, March 29)

Day 30 – Last day to obtain prescription
(Saturday, March 30)
# iPLEDGE Program Checklist

## BEFORE TREATMENT

### PLANNING

- Talk with your doctor/prescriber about isotretinoin and the iPLEDGE Program.
- Sign the Patient Information/Informed Consent (for all patients) form.
- Registration—ensure your doctor/prescriber registers you in the iPLEDGE Program.
- Get your patient ID card containing your patient ID number from your doctor/prescriber.
  - Keep your patient ID number in a safe place.
- Receive your password in the mail.

## PRESCRIPTION

- Obtain your prescription for up to a maximum of a 30-day supply.
  - Note: isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack and provide fewer than 10 capsules.
- Obtain your prescription using your iPLEDGE Program patient ID number within the 30-day prescription window counting your office visit as DAY 1.

## DURING TREATMENT

- Keep your appointments every month to get a prescription.
- Obtain your prescription using your iPLEDGE Program patient ID number within the 30-day prescription window counting the office visit as DAY 1. If you do not obtain your prescription within the 30-day prescription window, you will be required to start the process over again by visiting your doctor/prescriber.
- DO NOT donate blood.

## AFTER TREATMENT

- DO NOT share any leftover isotretinoin with anyone.
- DO NOT donate blood for 1 month after your last dose.

Web site: [www.ipledgeprogram.com](http://www.ipledgeprogram.com)
Phone system: 1-866-495-0654
Changing to a New Doctor/Prescriber

You can change your doctor/prescriber through the iPLEDGE® Program web site, www.ipledgeprogram.com by choosing “Change Primary Prescriber” from the menu or by calling 1-866-495-0654. Once you make the change, you will not be able to get any more prescriptions from your original doctor/prescriber.

See the Safety Information About Isotretinoin inside back pocket for more detailed information about other serious side effects, precautions, and warnings for isotretinoin.

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.
Patient Information/Informed Consent
Important form you must sign before you begin taking isotretinoin.

Patient Identification Cards
Remove one ID card and take it along with your prescription to the pharmacy (within your prescription window) to obtain your isotretinoin. Separate the cards and keep the duplicate ID card in a safe place.

Safety Information About Isotretinoin
Important information you should know about isotretinoin.
Patient Information/Informed Consent (for all patients):

To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.

Read each item below and initial in the space provided if you understand each item and agree to follow your doctor’s instructions. A parent or guardian of a patient under age 18 must also read and understand each item before signing the agreement.

Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I ___________________________ (Patient’s Name)
understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.

Initials: ______

2. My doctor has told me about my choices for treating my acne.

Initials: ______

3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. [Note: There is a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)].

Initials: ______

4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, “anxious” or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people have tried to end their own lives. And some people have ended their own lives. There were reports that many of these people did not appear depressed. There have been reports of patients on isotretinoin becoming aggressive or violent. No one knows if isotretinoin caused these behaviors or if they would have happened even if the person did not take isotretinoin. Some people have had other signs of depression while taking isotretinoin (see #7).

Initials: ______

5. Before I start taking isotretinoin, I agree to tell my doctor if I have ever had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.

Initials: ______

6. Before I start taking isotretinoin, I agree to tell my doctor if, to the best of my knowledge, anyone in my family has ever had symptoms of depression, been psychotic, attempted suicide, or had any other serious mental problems.

Initials: ______

7. Once I start taking isotretinoin, I agree to stop using isotretinoin and tell my doctor right away if any of the following signs and symptoms of depression or psychosis happen:

• Start to feel sad or have crying spells
• Lose interest in activities I once enjoyed
• Sleep too much or have trouble sleeping
• Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
• Have a change in my appetite or body weight
• Have trouble concentrating
• Withdraw from my friends or family
• Feel like I have no energy
• Have feelings of worthlessness or guilt
• Start having thoughts about hurting myself or taking my own life (suicidal thoughts)
• Start acting on dangerous impulses
• Start seeing or hearing things that are not real

Initials: ______

8. I agree to return to see my doctor every month I take isotretinoin to get a new prescription for isotretinoin, to check my progress, and to check for signs of side effects.

Initials: ______

9. Isotretinoin will be prescribed just for me — I will not share isotretinoin with other people because it may cause serious side effects, including birth defects.

Initials: ______

10. I will not give blood while taking isotretinoin or for 1 month after I stop taking isotretinoin. I understand that if someone who is pregnant gets my donated blood, her baby may be exposed to isotretinoin and may be born with serious birth defects.

Initials: ______

11. I have read the Patient Introductory Brochure and other materials my provider provided me containing important safety information about isotretinoin. I understand all the information I received.

Initials: ______

12. My doctor and I have decided I should take isotretinoin. I understand that I must be qualified in the iPLEDGE Program to have my prescription filled each month. I understand that I can stop taking isotretinoin at any time. I agree to tell my doctor if I stop taking isotretinoin.

Initials: ______

I now allow my doctor ___________________________ to begin my treatment with isotretinoin.

Patient Signature: ___________________________________________ Date: ___________________________

Parent/Guardian Signature (if under age 18): ___________________________ Date: ___________________________

Patient Address __________________________________________________________________ Telephone ___________________________

I have:

• fully explained to the patient, ___________________________, the nature and purpose of isotretinoin treatment, including its benefits and risks
• provided the patient the appropriate educational materials, such as the Patient Introductory Brochure and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin
• answered those questions to the best of my ability

Doctor Signature: ___________________________________________ Date: ___________________________

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT’S MEDICAL RECORD. PLEASE PROVIDE A COPY TO THE PATIENT.

www.ipledgeprogram.com | 1-866-495-0654
Women who can get pregnant must:
1. Have a monthly pregnancy test
2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654

Visit your doctor monthly
Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
Do not get pregnant
Do not share your drug
Do not donate blood

Stop isotretinoin and call your doctor right away if you are pregnant.
Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

See reverse for important safety information
What Is The Most Important Information I Should Know About Isotretinoin?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE® Program.
- Isotretinoin may cause serious mental health problems.

1. Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.

   Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor.

Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654
2. **Serious mental health problems.** Isotretinoin may cause:
   - Depression
   - Psychosis (seeing or hearing things that are not real)
   - Suicide

Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

**Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:**
   - Start to feel sad or have crying spells
   - Lose interest in activities you once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in your appetite or body weight
   - Have trouble concentrating
   - Withdraw from your friends or family
   - Feel like you have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

**What Is Isotretinoin?**

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See "**What is the most important information I should know about isotretinoin?**") Isotretinoin can only be:
   - Prescribed by doctors that are registered in the iPLEDGE® Program
   - Dispensed by a pharmacy that is registered with the iPLEDGE Program
   - Given to patients who are registered in the iPLEDGE Program and agree to do everything required in the Program

2
What Is Severe Nodular Acne?
Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?
- Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects. (See “What is the most important information I should know about isotretinoin?”)
- Do not take isotretinoin if you are allergic to anything in it.

What Should I Tell My Doctor Before Taking Isotretinoin?
Tell your doctor if you or a family member has any of the following health conditions:
- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:
- Vitamin A supplements. Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- Tetracycline antibiotics. Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.
• **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.

• **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.

• **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.

• **St. John’s Wort.** This herbal supplement may make birth control pills work less effectively.

**These medicines should not be used with isotretinoin unless your doctor tells you it is okay.**

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

**How Should I Take Isotretinoin?**

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE® Program.

Before prescribing isotretinoin, your doctor will:

• Explain the iPLEDGE Program to you.

• Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

**You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE Program.**

• You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE Program. You should talk with your doctor each month about side effects.

• The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.

• Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.

• If you miss a dose, just skip that dose. Do not take 2 doses at the same time.

• If you take too much isotretinoin or overdose, call your doctor or poison control center right away.

• Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
• You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.

• Female patients who can get pregnant must agree to use 2 separate methods of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE Program system to answer questions about the Program requirements and to enter your 2 chosen methods of birth control.** To access the iPLEDGE Program system, go to www.ipledgeprogram.com or call 1-866-495-0654.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this free visit, which will be paid for by the company that makes isotretinoin.

**If you have sex at any time without using 2 methods of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.**

### What Should I Avoid While Taking Isotretinoin?

• **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See **“What is the most important information I should know about isotretinoin?”**)

• **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.

• **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.

• **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See **“What should I tell my doctor before taking isotretinoin?”**)

• **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.
• Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop. Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.

• Avoid sunlight and ultraviolet lights as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.

• Do not share isotretinoin with other people. It can cause birth defects and other serious health problems.

What Are The Possible Side Effects of Isotretinoin?

• Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. (See “What is the most important information I should know about isotretinoin?”)

• Isotretinoin may cause serious mental health problems. (See “What is the most important information I should know about isotretinoin?”)

• Serious brain problems. Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  – Bad headache
  – Blurred vision
  – Dizziness
  – Nausea or vomiting
  – Seizures (convulsions)
  – Stroke

• Skin problems. Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like “pink eye”), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.

• Stomach area (abdomen) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach).
If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:

- Severe stomach, chest, or bowel pain
- Trouble swallowing or painful swallowing
- New or worsening heartburn
- Diarrhea
- Rectal bleeding
- Yellowing of your skin or eyes
- Dark urine

**Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin.

Tell your doctor if you get:

- Back pain
- Joint pain
- A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

**Stop isotretinoin and call your doctor right away if you have muscle weakness.** Muscle weakness with or without pain can be a sign of serious muscle damage. Isotretinoin may stop long bone growth in teenagers who are still growing.

**Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.

**Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.

**Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
• **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.

• **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.

• **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.

• **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

**Call your doctor for medical advice about side effects.** You may report side effects to FDA at 1-800-FDA-1088.

### How Should I Store Isotretinoin?

• Store isotretinoin at room temperature. Protect from light.

• **Keep isotretinoin and all medicines out of the reach of children.**

### General Information About Isotretinoin

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for healthcare professionals. You can also call iPLEDGE® Program at 1-866-495-0654 or visit [www.ipledgeprogram.com](http://www.ipledgeprogram.com).
1. Visit your doctor/prescriber monthly
2. Women who can get pregnant must:
   1. Have a monthly pregnancy test
   2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
   3. Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
   4. Do not get pregnant
   5. Do not share your drug
   6. Do not donate blood

See reverse for important safety information

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.
Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Are you thinking about taking isotretinoin (eye-soh-tret-in-OH-in) for acne? Read this brochure to learn more about isotretinoin and the iPLEDGE Program.

WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.

Obtain isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
What Is Isotretinoin?

Isotretinoin (eye-soh-tret-in-OH-in) is a prescription medication that treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months. Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby’s mother takes isotretinoin. You should also learn about the side effects and the precautions and warnings (see the enclosed sheet entitled Safety Information About Isotretinoin). Talk with your doctor about how bad your acne is and how isotretinoin can help your skin. Decide if isotretinoin is right for you. Your doctor will ask you to read and sign forms that say you understand the serious risks of isotretinoin. It is important for you to know how to take isotretinoin correctly and what to expect.
What Is The iPLEDGE® Program?

The iPLEDGE Program is a set of steps all patients, doctors/prescribers, and pharmacists must follow. The main goal is preventing pregnancy and birth defects, but both male patients and female patients must follow the iPLEDGE Program. To avoid serious risks to unborn babies, the Food and Drug Administration (FDA) has required a special Program called a Risk Evaluation and Mitigation Strategy (REMS) for isotretinoin. The iPLEDGE Program is a single, shared (includes multiple manufacturers) system with requirements for prescribers, pharmacies, and patients. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to

- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Only registered and activated prescribers can prescribe isotretinoin and only registered and activated pharmacies can dispense isotretinoin. In order to receive isotretinoin, all patients must be enrolled in the iPLEDGE Program and agree to follow the requirements. All patients must:

- Sign the Patient Information/Informed Consent form(s)
- Be able to keep appointments
- Agree to follow the iPLEDGE Program steps
Safety Information About Isotretinoin

What Is The Most Important Information I Should Know About Isotretinoin?

• Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
• Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPledge® Program.
• Isotretinoin may cause serious mental health problems.

1. Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.

   Female patients must not get pregnant:
   • For 1 month before starting isotretinoin
   • While taking isotretinoin
   • For 1 month after stopping isotretinoin

   If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:
   • FDA MedWatch at 1-800-FDA-1088, and
   • The iPledge Program Pregnancy Registry at 1-866-495-0654

2. Serious mental health problems. Isotretinoin may cause:
   • Depression
   • Psychosis (seeing or hearing things that are not real)
   • Suicide

Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.
Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

**What Is Isotretinoin?**

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See “[What is the most important information I should know about isotretinoin?](https://www.iPLEDGE.com)”) Isotretinoin can only be:

- Prescribed by doctors that are registered in the iPLEDGE Program
- Dispensed by a pharmacy that is registered with the iPLEDGE Program
- Given to patients who are registered in the iPLEDGE Program and agree to do everything required in the Program

**What Is Severe Nodular Acne?**

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.
Who Should Not Take Isotretinoin?

- Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects. (See “What is the most important information I should know about isotretinoin?”)
- Do not take isotretinoin if you are allergic to anything in it.

What Should I Tell My Doctor Before Taking Isotretinoin?

Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- **Vitamin A supplements.** Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- **Tetracycline antibiotics.** Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.
- **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.
- **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.
- **St. John's Wort.** This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.
How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE® Program. Before prescribing isotretinoin, your doctor will:

• Explain the iPLEDGE Program to you.
• Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE Program.

• You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE Program. You should talk with your doctor each month about side effects.
• The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
• Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
• If you miss a dose, just skip that dose. Do not take 2 doses at the same time.
• If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
• Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
• You must return to your doctor as directed to make sure you don’t have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.
• Female patients who can get pregnant must agree to use 2 separate methods of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE Program system to answer questions about the Program requirements and to enter your 2 chosen methods of birth control.** To access the iPLEDGE Program system, go to [www.ipledgeprogram.com](http://www.ipledgeprogram.com) or call 1-866-495-0654.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this free visit, which will be paid for by the company that makes isotretinoin.

**If you have sex at any time without using 2 methods of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.**
What Should I Avoid While Taking Isotretinoin?

- Do not get pregnant while taking isotretinoin and for 1 month after stopping isotretinoin. (See “What is the most important information I should know about isotretinoin?”)
- Do not breastfeed while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.
- Do not give blood while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.
- Do not take other medicines or herbal products with isotretinoin unless you talk to your doctor. (See “What should I tell my doctor before taking isotretinoin?”)
- Do not drive at night until you know if isotretinoin has affected your vision. Isotretinoin may decrease your ability to see in the dark.
- Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop. Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.
- Avoid sunlight and ultraviolet lights as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.
- Do not share isotretinoin with other people. It can cause birth defects and other serious health problems.

What Are The Possible Side Effects of Isotretinoin?

- Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. (See “What is the most important information I should know about isotretinoin?”)
- Isotretinoin may cause serious mental health problems. (See “What is the most important information I should know about isotretinoin?”)
- Serious brain problems. Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  - Bad headache
  - Blurred vision
  - Dizziness
  - Nausea or vomiting
  - Seizures (convulsions)
  - Stroke
• **Skin problems.** Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like “pink eye”), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.

• **Stomach area (abdomen) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach).

   If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:
   - Severe stomach, chest, or bowel pain
   - Trouble swallowing or painful swallowing
   - New or worsening heartburn
   - Diarrhea
   - Rectal bleeding
   - Yellowing of your skin or eyes
   - Dark urine

• **Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:
   - Back pain
   - Joint pain
   - A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

   **Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.**

   Isotretinoin may stop long bone growth in teenagers who are still growing.

• **Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.

• **Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.

• **Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
What Are The Possible Side Effects of Isotretinoin? (Cont.)

- **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.
  - **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.
  - **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.
  - **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

**Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.**

**How Should I Store Isotretinoin?**

- Store isotretinoin at room temperature. Protect from light.
- Keep isotretinoin and all medicines out of the reach of children.

**General Information About Isotretinoin**

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for healthcare professionals. You can also call iPLEDGE® Program at 1-866-495-0654 or visit www.ipledgeprogram.com.
Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.
WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
The tools you need to help you prepare and plan treatments during the course of isotretinoin treatment

**WARNING**
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

**IMPORTANT NOTICE**
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

CAUSES
BIRTH DEFECTS
DO NOT GET PREGNANT
TABLE OF CONTENTS

Guide for Male Patients and Female Patients Who Cannot Get Pregnant ........ 4

iPLEDGE® Program Checklist ........................................................................ 7

Patient Information/Informed Consent (for all patients) .............................. 11*

Safety Information About Isotretinoin ........................................................ 11*

Patient Identification Cards ....................................................................... 11*

*Located inside back cover pocket.
What Is Isotretinoin?

Isotretinoin (eye-soh-tret-in-OH-in) is a prescription medication that treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months. Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby’s mother takes isotretinoin. You should also learn about the side effects and the precautions and warnings (see the enclosed sheet entitled Safety Information About Isotretinoin).

What Is The iPLEDGE® Program?

To avoid serious risks to unborn babies, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for isotretinoin. The iPLEDGE Program is a single, shared (includes multiple manufacturers) system with requirements for prescribers, pharmacies, and patients. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to

- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Only registered and activated prescribers can prescribe isotretinoin and only registered and activated pharmacies can dispense isotretinoin. In order to receive isotretinoin, all patients must be enrolled in the iPLEDGE Program and agree to follow the requirements.
What Do All Patients Need To Know?

Prevent Pregnancy and Birth Defects

There is a very high chance that babies born to female patients taking isotretinoin will be deformed, born too early, or die before they are born. This can happen even if a female patient takes isotretinoin for only a short time. It may also happen if a pregnant female receives a blood transfusion from someone taking isotretinoin.

Do male patients taking isotretinoin need to worry about birth defects?

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin.

If you are worried about isotretinoin birth defects from sperm, you can use a male latex condom to help prevent pregnancy. Use a condom each and every time you have intercourse (sex) while you are taking isotretinoin and for 1 month after you stop taking it.

Can isotretinoin affect a male patient’s ability to father healthy children?

Studies on isotretinoin did not show effects on sperm count, how sperm look, or how well they swim and move.

Do Not Donate Blood

Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant female gets blood from you. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone

You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

Obtain Your Prescription

Obtain your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

The web site, www.ipledgeprogram.com, has a list of registered pharmacies. Once on the web site choose “Find a Participating Pharmacy” in the left navigation. A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.
What Do Male Patients And Female Patients Who Cannot Get Pregnant Need To Know?

You can only obtain isotretinoin if:

- You are registered in the iPLEDGE® Program, your doctor/prescriber has entered your patient information in the iPLEDGE Program system, and you have your patient ID number.

- You must obtain the prescription within the 30-day prescription window, counting the office visit as DAY 1. The 30-day prescription window expires at 11:59 p.m. Eastern Time on Day 30 of the prescription window.

The iPLEDGE Program system will automatically compute the “Do Not Dispense To Patient After” date for your pharmacist.

To figure out the last date you can obtain your prescription, add 29 days to the date of your office visit. For example:

- **Day 1 and Day of the office visit**
  - (Friday, March 1)

- **Day 2 – Day 29**
  - (Saturday, March 2 thru Friday, March 29)

- **Day 30 – Last day to obtain prescription**
  - (Saturday, March 30)
iPLEDGE Program Checklist

BEFORE TREATMENT

PLANNING

☐ Talk with your doctor/prescriber about isotretinoin and the iPLEDGE Program.
☐ Sign the Patient Information/Informed Consent (for all patients) form.
☐ Registration—ensure your doctor/prescriber registers you in the iPLEDGE Program.
☐ Get your patient ID card containing your patient ID number from your doctor/prescriber. Keep your patient ID number in a safe place.
☐ Receive your password in the mail.

PRESCRIPTION

☐ Obtain your prescription for up to a maximum of a 30-day supply.
  • Note: isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack and provide fewer than 10 capsules.
☐ Obtain your prescription using your iPLEDGE Program patient ID number within the 30-day prescription window counting your office visit as DAY 1.

DURING TREATMENT

☐ Keep your appointments every month to get a prescription.
☐ Obtain your prescription using your iPLEDGE Program patient ID number within the 30-day prescription window counting the office visit as DAY 1. If you do not obtain your prescription within the 30-day prescription window, you will be required to start the process over again by visiting your doctor/prescriber.
☐ DO NOT donate blood.

AFTER TREATMENT

☐ DO NOT share any leftover isotretinoin with anyone.
☐ DO NOT donate blood for 1 month after your last dose.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
Changing to a New Doctor/Prescriber

You can change your doctor/prescriber through the iPLEDGE® Program web site, www.ipledgeprogram.com by choosing “Change Primary Prescriber” from the menu or by calling 1-866-495-0654. Once you make the change, you will not be able to get any more prescriptions from your original doctor/prescriber.

See the Safety Information About Isotretinoin inside back pocket for more detailed information about other serious side effects, precautions, and warnings for isotretinoin.

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.
Patient Information/Informed Consent
Important form you must sign before you begin taking isotretinoin.

Patient Identification Cards
Remove one ID card and take it along with your prescription to the pharmacy (within your prescription window) to obtain your isotretinoin. Separate the cards and keep the duplicate ID card in a safe place.

Safety Information About Isotretinoin
Important information you should know about isotretinoin.
Patient Information/Informed Consent (for all patients):

To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.

Read each item below and initial in the space provided if you understand each item and agree to follow your doctor's instructions. A parent or guardian of a patient under age 18 must also read and understand each item before signing the agreement.

Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I, ____________________________ (Patient's Name)
   understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.
   Initials: ______

2. My doctor has told me about my choices for treating my acne.
   Initials: ______

3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. (Note: There is a second Patient Information/Informed Consent About Birth Defects for female patients who can get pregnant).
   Initials: ______

4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, "anxious" or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives. There were reports that some of these people did not appear depressed. There have been reports of patients on isotretinoin becoming aggressive or violent. No one knows if isotretinoin caused these behaviors or if they would have happened even if the person did not take isotretinoin. Some people have had other signs of depression while taking isotretinoin (see #7).
   Initials: ______

5. Before I start taking isotretinoin, I agree to tell my doctor if I have ever had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.
   Initials: ______

6. Before I start taking isotretinoin, I agree to tell my doctor if, to the best of my knowledge, anyone in my family has ever had symptoms of depression, been psychotic, attempted suicide, or had any other serious mental problems.
   Initials: ______

7. Once I start taking isotretinoin, I agree to stop using isotretinoin and tell my doctor right away if any of the following signs and symptoms of depression or psychosis happen. I:
   - Start to feel sad or have crying spells
   - Lose interest in activities I once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in my appetite or body weight
   - Have trouble concentrating
   - Withdraw from my friends or family
   - Feel like I have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting myself or taking my own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real
   Initials: ______

8. I agree to return every month I take isotretinoin to get a new prescription for isotretinoin, to check my progress, and to check for signs of side effects.
   Initials: ______

9. Isotretinoin will be prescribed just for me — I will not share isotretinoin with other people because it may cause serious side effects, including birth defects.
   Initials: ______

10. I will not give blood while taking isotretinoin or for 1 month after I stop taking isotretinoin. I understand that if someone who is pregnant gets my donated blood, her baby may be exposed to isotretinoin and may be born with serious birth defects.
    Initials: ______

11. I have read the Patient Introductory Brochure and other materials my provider provided me containing important safety information about isotretinoin. I understand all the information I received.
    Initials: ______

12. My doctor and I have decided I should take isotretinoin. I understand that I must be qualified in the iPLEDGE Program to have my prescription filled each month. I understand that I can stop taking isotretinoin at any time. I agree to tell my doctor if I stop taking isotretinoin.
    Initials: ______

I now allow my doctor ____________________________ to begin my treatment with isotretinoin.

Patient Signature: ____________________________ Date: ________________
Parent/Guardian Signature (if under age 18): ____________________________ Date: ________________
Patient Address __________________________________________________________ Telephone ________________

I have:
- fully explained to the patient, ____________________________________________________, the nature and purpose of isotretinoin treatment, including its benefits and risks
- provided the patient the appropriate educational materials, such as the Patient Introductory Brochure and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin
- answered those questions to the best of my ability

Doctor Signature: ____________________________ Date: ________________

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT’S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.
• Visit your doctor monthly
• Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
• Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
• Do not get pregnant
• Do not share your drug
• Do not donate blood

Stop isotretinoin and call your doctor right away if you are pregnant.
Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

• Start to feel sad or have crying spells
• Lose interest in activities you once enjoyed
• Sleep too much or have trouble sleeping
• Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
• Have a change in your appetite or body weight
• Have trouble concentrating
• Withdraw from your friends or family
• Feel like you have no energy
• Have feelings of worthlessness or guilt
• Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
• Start acting on dangerous impulses
• Start seeing or hearing things that are not real

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Reference ID: 4252185
What Is The Most Important Information I Should Know About Isotretinoin?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.

- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE® Program.

- Isotretinoin may cause serious mental health problems.

1. Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.

   Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654
2. **Serious mental health problems.** Isotretinoin may cause:
   - Depression
   - Psychosis (seeing or hearing things that are not real)
   - Suicide

Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

**Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:**
   - Start to feel sad or have crying spells
   - Lose interest in activities you once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in your appetite or body weight
   - Have trouble concentrating
   - Withdraw from your friends or family
   - Feel like you have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

**What Is Isotretinoin?**

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See “**What is the most important information I should know about isotretinoin?**”) Isotretinoin can only be:
   - Prescribed by doctors that are registered in the iPLEDGE® Program
   - Dispensed by a pharmacy that is registered with the iPLEDGE Program
   - Given to patients who are registered in the iPLEDGE Program and agree to do everything required in the Program
What Is Severe Nodular Acne?
Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?

- Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects. (See “What is the most important information I should know about isotretinoin?”)
- Do not take isotretinoin if you are allergic to anything in it.

What Should I Tell My Doctor Before Taking Isotretinoin?
Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- Vitamin A supplements. Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- Tetracycline antibiotics. Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.

Reference ID: 4252185
• Progestin-only birth control pills (mini-pills). They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.

• Dilantin (phenytoin). This medicine taken with isotretinoin may weaken your bones.

• Corticosteroid medicines. These medicines taken with isotretinoin may weaken your bones.

• St. John’s Wort. This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE® Program. Before prescribing isotretinoin, your doctor will:

• Explain the iPLEDGE Program to you.

• Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE Program.

• You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE Program. You should talk with your doctor each month about side effects.

• The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.

• Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule. Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.

• If you miss a dose, just skip that dose. Do not take 2 doses at the same time.

• If you take too much isotretinoin or overdose, call your doctor or poison control center right away.

• Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.
• You must return to your doctor as directed to make sure you don’t have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.

• Female patients who can get pregnant must agree to use 2 separate methods of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE Program system to answer questions about the Program requirements and to enter your 2 chosen methods of birth control.** To access the iPLEDGE Program system, go to [www.ipledgeprogram.com](http://www.ipledgeprogram.com) or call 1-866-495-0654.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this free visit, which will be paid for by the company that makes isotretinoin.

**If you have sex at any time without using 2 methods of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.**

### What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See “**What is the most important information I should know about isotretinoin?**”)

- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.

- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.

- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See “**What should I tell my doctor before taking isotretinoin?**”)

- **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.
• Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop. Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.

• Avoid sunlight and ultraviolet lights as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.

• Do not share isotretinoin with other people. It can cause birth defects and other serious health problems.

What Are The Possible Side Effects of Isotretinoin?

• Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. (See “What is the most important information I should know about isotretinoin?”)

• Isotretinoin may cause serious mental health problems. (See “What is the most important information I should know about isotretinoin?”)

• Serious brain problems. Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  – Bad headache
  – Blurred vision
  – Dizziness
  – Nausea or vomiting
  – Seizures (convulsions)
  – Stroke

• Skin problems. Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like “pink eye”), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.

• Stomach area (abdomen) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach).
If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:

- Severe stomach, chest, or bowel pain
- Trouble swallowing or painful swallowing
- New or worsening heartburn
- Diarrhea
- Rectal bleeding
- Yellowing of your skin or eyes
- Dark urine

**Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:

- Back pain
- Joint pain
- A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage. Isotretinoin may stop long bone growth in teenagers who are still growing.

**Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.

**Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.

**Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
• **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.

• **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.

• **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.

• **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

**Call your doctor for medical advice about side effects.**

You may report side effects to FDA at 1-800-FDA-1088.

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**How Should I Store Isotretinoin?**

• Store isotretinoin at room temperature. Protect from light.

• **Keep isotretinoin and all medicines out of the reach of children.**

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**General Information About Isotretinoin**

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for healthcare professionals. You can also call iPLEDGE® Program at 1-866-495-0654 or visit www.i pledgeprogram.com.
• Visit your doctor/prescriber monthly
• Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
• Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
• Do not get pregnant
• Do not share your drug
• Do not donate blood

See reverse for important safety information

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

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WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.
Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
The tools you need to help you prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment.

WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin can cause severe birth defects (deformed babies), loss of a baby (miscarriage), death of a baby, and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
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Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
• Safety Information About Isotretinoin
• iPLEDGE® Program Birth Control Information Sheet/iPLEDGE Program Checklist
• Birth Control Workbook
- Guide to Isotretinoin For Female Patients Who Can Get Pregnant
  - Patient Identification Cards
  - Patient Information/Informed Consent About Birth Defects
- Contraception Counseling Guide And Contraception Referral Form
What Is The Most Important Information I Should Know About Isotretinoin?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE® Program.
- Isotretinoin may cause serious mental health problems.

1. Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.

   Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

   If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor.

Doctors and patients should report all cases of pregnancy to:
- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654

Reference ID: 4252185
2. Serious mental health problems. Isotretinoin may cause:
   - Depression
   - Psychosis (seeing or hearing things that are not real)
   - Suicide

Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

   - Start to feel sad or have crying spells
   - Lose interest in activities you once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in your appetite or body weight
   - Have trouble concentrating
   - Withdraw from your friends or family
   - Feel like you have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

What Is Isotretinoin?

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See “What is the most important information I should know about isotretinoin?”) Isotretinoin can only be:

   - Prescribed by doctors that are registered in the iPLEDGE* Program
   - Dispensed by a pharmacy that is registered with the iPLEDGE Program
   - Given to patients who are registered in the iPLEDGE Program and agree to do everything required in the Program
What Is Severe Nodular Acne?
Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?
- Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects. (See “What is the most important information I should know about isotretinoin?”)
- Do not take isotretinoin if you are allergic to anything in it.

What Should I Tell My Doctor Before Taking Isotretinoin?
Tell your doctor if you or a family member has any of the following health conditions:
- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:
- Vitamin A supplements. Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- Tetracycline antibiotics. Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.

Reference ID: 4252185
- Progestin-only birth control pills (mini-pills). They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- Dilantin (phenytoin). This medicine taken with isotretinoin may weaken your bones.
- Corticosteroid medicines. These medicines taken with isotretinoin may weaken your bones.
- St. John’s Wort. This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE® Program. Before prescribing isotretinoin, your doctor will:

- Explain the iPLEDGE Program to you.
- Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE Program.

- You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE Program. You should talk with your doctor each month about side effects.
- The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
- Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule. Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
- If you miss a dose, just skip that dose. Do not take 2 doses at the same time.
- If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
- Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
You must return to your doctor as directed to make sure you don’t have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.

Female patients who can get pregnant must agree to use 2 separate methods of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. You must access the iPLEDGE Program system to answer questions about the Program requirements and to enter your 2 chosen methods of birth control. To access the iPLEDGE Program system, go to www.ipledgeprogram.com or call 1-866-495-0654.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this free visit, which will be paid for by the company that makes isotretinoin.

If you have sex at any time without using 2 methods of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.

What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See “What is the most important information I should know about isotretinoin?”)

- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.

- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.

- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See “What should I tell my doctor before taking isotretinoin?”)

- **Do not drive at night** until you know if isotretinoin has affected your vision. Isotretinoin may decrease your ability to see in the dark.
• Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop. Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.

• Avoid sunlight and ultraviolet lights as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.

• Do not share isotretinoin with other people. It can cause birth defects and other serious health problems.

What Are The Possible Side Effects of Isotretinoin?

• Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. (See “What is the most important information I should know about isotretinoin?”)

• Isotretinoin may cause serious mental health problems. (See “What is the most important information I should know about isotretinoin?”)

• Serious brain problems. Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  – Bad headache
  – Blurred vision
  – Dizziness
  – Nausea or vomiting
  – Seizures (convulsions)
  – Stroke

• Skin problems. Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like “pink eye”), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.

• Stomach area (abdomen) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach).
If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:

- Severe stomach, chest, or bowel pain
- Trouble swallowing or painful swallowing
- New or worsening heartburn
- Diarrhea
- Rectal bleeding
- Yellowing of your skin or eyes
- Dark urine

**Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:

- Back pain
- Joint pain
- A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Isotretinoin may stop long bone growth in teenagers who are still growing.

**Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.

**Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.

**Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
• **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.

• **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.

• **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.

• **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

**Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.**

**How Should I Store Isotretinoin?**

• Store isotretinoin at room temperature. Protect from light.

• Keep isotretinoin and all medicines out of the reach of children.

**General Information About Isotretinoin**

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for healthcare professionals. You can also call iPLEDGE® Program at 1-866-495-0654 or visit www.ipledgeprogram.com.
**iPLEDGE® Program Birth Control Information Sheet**

Choose 1 Primary + 1 Secondary Birth Control Method

<table>
<thead>
<tr>
<th>Primary Method of Birth Control (Choose One)*</th>
<th>How to Use it</th>
<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormonal Implant</strong></td>
<td>Placed under skin of arm by a clinician. Works for 3 years.¹</td>
<td>&gt;99%¹</td>
<td>• Nothing to do or remember • Light or no periods • May decrease acne • No increased risk of clots</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td><strong>Hormonal IUD</strong></td>
<td>Placed in uterus by clinician. Self-check monthly. Works for 5 years.¹</td>
<td>&gt;99%¹</td>
<td>• Light or no periods • No increased risk of clots</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td><strong>Non-Hormonal IUD</strong></td>
<td>Placed in uterus by a clinician. Self-check monthly. Works for 10 years.³</td>
<td>&gt;99%¹</td>
<td>• No hormones • Periods remain regular • Effective immediately • No increased risk of clots</td>
<td>May cause heavier periods and cramping</td>
</tr>
<tr>
<td><strong>Tubal Sterilization</strong></td>
<td>Surgical procedure to close the tubes between the uterus and the ovaries.</td>
<td>&gt;99%²</td>
<td>• It is a virtually permanent method of birth control • Nothing to do or remember</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
</tr>
<tr>
<td><strong>Male Vasectomy</strong></td>
<td>Surgical procedure that closes off the tubes that carry a partner's sperm.</td>
<td>&gt;99%²</td>
<td>• It is a virtually permanent method of birth control • Nothing to do or remember</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
</tr>
<tr>
<td><strong>Hormonal Shot</strong></td>
<td>Given every 3 months by a clinician.</td>
<td>&gt;97%¹</td>
<td>• Light or no periods • No increased risk of clots</td>
<td>Irregular Periods • May cause weight gain</td>
</tr>
<tr>
<td><strong>Vaginal Ring</strong></td>
<td>You place in vagina. Replace monthly.</td>
<td>92%¹</td>
<td>• Lighter periods • May decrease acne</td>
<td>Blood clots</td>
</tr>
<tr>
<td><strong>Hormonal Patch</strong></td>
<td>You place on skin. Replace weekly.</td>
<td>92%¹</td>
<td>• Lighter periods • May decrease acne</td>
<td>Blood clots</td>
</tr>
<tr>
<td><strong>Birth Control Pill (Combination Type)</strong></td>
<td>Swallow at the same time daily.</td>
<td>92%¹</td>
<td>• Lighter periods • May decrease acne</td>
<td>Blood clots</td>
</tr>
</tbody>
</table>

**Secondary Method of Birth Control (Choose One)**

<table>
<thead>
<tr>
<th>How to Use it</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Condoms (with or without spermicide)</strong></td>
<td>Partner must be willing to use each and every time you have sex.</td>
<td>Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS</td>
</tr>
<tr>
<td><strong>Cervical Cap, Diaphragm</strong> (must be used with spermicide). Vaginal Sponge</td>
<td>Place in vagina before you have sex.</td>
<td>You are in control of its use</td>
</tr>
</tbody>
</table>

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.

Abstinence means that you commit to not having sex or sexual contact with any male 24 hours a day, 7 days a week for 1 month before, during, and for 1 month after your isotretinoin treatment.

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*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.
†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.
BEFORE TREATMENT

PLANNING
☐ Talk with your doctor about isotretinoin and the iPLEDGE Program
☐ Sign the Patient Information/Informed Consent (for all patients) form
☐ Sign the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
☐ Have your first urine or blood pregnancy test, which can be performed at the doctor's office
☐ Registration—ensure your doctor registers you in the iPLEDGE Program. You must be registered for at least 30 days prior to your first prescription.
☐ Get your patient ID card containing your patient ID number from your doctor. Keep your patient ID number in a safe place.
☐ Receive your password in the mail

BIRTH CONTROL
☐ Read the enclosed Birth Control Information Sheet and for additional information on birth control options read the enclosed Birth Control Workbook
☐ Talk with your dermatologist, gynecologist, family doctor, or a birth control expert about effective birth control options
☐ Choose 2 effective methods of birth control
☐ Start using the 2 methods of birth control together for at least 1 month before you start isotretinoin

YOUR FIRST PRESCRIPTION
☐ Have a second pregnancy test conducted at an approved lab within the first 5 days of your menstrual period (at least 30 days after registration)
☐ Answer questions about the iPLEDGE Program and confirm your 2 methods of birth control
  • Note: you can answer your comprehension questions only after your doctor has entered your pregnancy test result in the iPLEDGE Program system
☐ Obtain your prescription for up to a maximum of a 30-day supply
  • Note: Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack and provide fewer than 10 capsules
☐ Obtain your prescription within the 7-day prescription window, counting the day of the pregnancy test as DAY 1
  • If you do not obtain your prescription within the 7-day prescription window, you will need to go back to your doctor to start this process again
☐ Obtain your prescription within the 7-day prescription window, counting the day of the pregnancy test as DAY 1
  • If you do not obtain your prescription within the 7-day prescription window, you will need to go back to your doctor to start this process again
☐ Do not donate blood

DURING TREATMENT
☐ Use 2 effective methods of birth control together all the time
☐ See your doctor for a monthly pregnancy test
☐ Keep your appointments every month to get a prescription
☐ Confirm your 2 methods of birth control by entering them into the iPLEDGE Program System
☐ Answer different questions each month about the iPLEDGE Program
  • Note: you can answer your comprehension questions only after your doctor has entered your pregnancy test result in the iPLEDGE Program system
☐ Obtain your prescription for up to a maximum of a 30-day supply
☐ Obtain your prescription within the 7-day prescription window counting the day of the pregnancy test as DAY 1
☐ Confirm that your doctor has entered the results of this pregnancy test into the iPLEDGE Program System
☐ Do not donate blood for 1 month after your last dose

AFTER TREATMENT

RIGHT AFTER YOUR LAST DOSE
☐ Get a pregnancy test after your last dose
☐ Confirm that your doctor has entered the results of this pregnancy test into the iPLEDGE Program System
☐ Continue using your 2 methods of birth control for 1 month
☐ Do not share any leftover isotretinoin with anyone
☐ Do not donate blood for 1 month after your last dose

ONE MONTH AFTER YOUR LAST DOSE
☐ Have a final pregnancy test at 1 month after your last dose
☐ Confirm that your doctor has entered the results of this pregnancy test into the iPLEDGE Program System

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
The iPLEDGE Program

Birth Control Workbook

The guide to help you decide which methods of birth control are best for you during treatment with isotretinoin

WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.

Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

Reference ID: 4252185
Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

CAUSES

BIRTH DEFECTS

DO NOT GET PREGNANT
# TABLE OF CONTENTS

- Preventing Pregnancies ................................................................. 4
- Why Should I Use This Workbook? .................................................. 5
- How Should I Use This Workbook? .................................................. 6
- The iPLEDGE® Program And Birth Control ........................................ 6
- Making a Choice About Birth Control ............................................... 11
- Primary Methods of Birth Control .................................................... 12
- Secondary Methods of Control ....................................................... 24
- Emergency Birth Control (Emergency Contraception) ...................... 31
- Reasons Female Patients Get Pregnant ............................................. 32
- Recognizing Pregnancy ................................................................. 33
Preventing Pregnancies

Not all methods of birth control are effective while you are taking isotretinoin. Choosing birth control is a very personal decision. It helps to get all the information you need and then talk with your doctor/prescriber to help you decide what to do.

Read This Birth Control Workbook

To find out which birth control is effective for the iPLEDGE® Program, read this *Birth Control Workbook*. Read it before you make any decisions about birth control. Read it even if you are already using birth control. Read it even if you think you will not have sex with a male for your whole isotretinoin treatment.

After you have read through the booklet, talk it over with someone you trust. Think about which methods of birth control you would really use. Then talk with your doctor/prescriber or a birth control expert.

Share this workbook with your partner. Talk with your partner about how to use the birth control methods you choose and about birth defects and isotretinoin. Explain what you both need to do to prevent pregnancy. Tell him you need to prevent pregnancy for at least 1 month before you start isotretinoin, during your treatment, and for 1 month after your last dose. You may need to take isotretinoin for several months.

Write down a list of questions for your dermatologist, gynecologist, or family doctor. No question is too silly. Make sure you know how to use the birth control methods you choose.
Why Should I Use This Workbook?

You are getting ready to start isotretinoin (eye-soh-tret-in-OH-in). It treats severe acne, but it can also cause birth defects. You must not get pregnant right before starting isotretinoin, while taking it, and for 1 month after your last dose. There is a very high chance that your baby could be deformed, born too early, or die. This can happen even if you take isotretinoin for only a short time.

![Birth Defects Diagram]

The pictures show some of the birth defects your baby can have. Your baby's head could be deformed; the ears could be an odd shape or even missing. The eyes could be too far apart, the bridge of the nose too low, or the chin smaller than normal. The baby could have mental retardation or severe problems in the glands, heart, and brain.

You do not want to be pregnant or get pregnant right before starting isotretinoin, while taking it, and for 1 month after your last dose.

To keep from getting pregnant, you need to use 2 effective methods of birth control together correctly all the time:

- For at least 1 month before you start isotretinoin
- During treatment which usually lasts 4 to 5 months
- For 1 month after your last dose—to continue protection against pregnancy

This workbook is for ALL female patients who can possibly get pregnant. This means that:

- You are physically able to get pregnant
- You have a uterus and ovaries
- You have menstrual periods

Even if you are not having sex, you still need to follow the requirements of the iPLEDGE Program.
Female Patients Who Cannot Get Pregnant

Female patients who cannot get pregnant are not required to be on birth control. This applies to you if:

- You have entered menopause, and your doctor/prescriber has confirmed this
- You do not have either of your 2 ovaries and/or a uterus, and your doctor/prescriber has confirmed this

If you have any questions about being able to get pregnant, talk with your doctor/prescriber.

How Should I Use This Workbook?

Use this workbook as a guide to help you decide which 2 effective birth control methods are best for you during your treatment. You will want to pick a birth control method that works for you and gives you the best protection against pregnancy (primary method). Since all methods of birth control can fail, you must also pick a second method (another primary method or a secondary method) that you use every time you have sex.

This workbook also provides information about abstinence, emergency birth control, and issues around conception and pregnancy.

The iPLEDGE® Program And Birth Control

Referree for birth control counseling

Before beginning treatment, you or the doctor/prescriber may choose a referral to a birth control expert. The makers of isotretinoin will pay for 1 visit for birth control counseling. The patient educational kit contains the Contraception Counseling Guide And Contraception Referral Form. The referral form is in the pocket of the Contraception Counseling Guide And Contraception Referral Form booklet. The Contraception Counseling Guide outlines the birth control requirements and the effective methods of birth control of the iPLEDGE Program for the birth control expert. The referral form should be filled out by your doctor/prescriber and taken with you to the birth control counselor.
Why Do I Have To Use 2 Methods of Birth Control Together?

- Any single birth control method can fail
- Using 2 methods of birth control together all the time drastically reduces the chance that you will get pregnant
- Most female patients who got pregnant during isotretinoin treatment were using only 1 method of birth control!

Can I Use Any 2 Methods of Birth Control?

No, you must choose from the iPLEDGE Program list of effective birth control methods. The 2 types of birth control you use for the iPLEDGE Program are called primary methods and secondary methods.

- **Primary methods** do not fail very often. Be sure to choose a primary method that gives you the lowest chance of failure. This depends on such things as how well you remember to take medicine every day, whether your partner has had a vasectomy, or you have any medical conditions.

- **Secondary methods** include barrier methods and other methods of birth control. The most important thing about a secondary method is using it every time you have sex.
  - **Barrier methods** keep sperm from entering the uterus. Barrier methods include the diaphragm and the cervical cap, both of which must be used with a cream that kills sperm, called a spermicide. The male latex condom is also a barrier method, and it can be used with or without spermicide.
  - **Other methods** (vaginal sponge) contain spermicide.

Preventing Pregnancy by Abstinence (Not Having Sex)

Abstinence means that you commit to not having sex or sexual contact with any male 24 hours a day, 7 days a week for 1 month before, during, and for 1 month after your isotretinoin treatment. This can be hard to do, especially if you have previously been sexually active.

It is easier not to have sex when it is a lifestyle choice, such as religious practice. One of the most common causes of unplanned pregnancy is not being able to avoid sex (failing to maintain abstinence).

If you cannot commit completely to not having sex (abstinence) while taking isotretinoin, you MUST contact your prescriber before engaging in sexual activity. You must not take isotretinoin if you cannot follow the birth control requirements of the iPLEDGE Program.
Concerns About Birth Control Pills

Many female patients use birth control pills. But birth control pills can fail, and you can get pregnant. They usually fail because you may forget to take them as directed by your healthcare provider.

- If you take them about the same time every day, they are very effective birth control
- If you miss pills and do not take them every day, your chance of getting pregnant is much higher with birth control pills than with other primary birth control methods, such as hormonal shots or an intrauterine device (IUD)

If you are taking birth control pills, do you remember to take them every day? If not you need to consider another primary method of birth control as you read this workbook.
### Program Approved Methods of Contraception

Choose 1 Primary + 1 Secondary Birth Control Method

<table>
<thead>
<tr>
<th>Primary Method of Birth Control  (Choose One)*</th>
<th>How to Use it</th>
<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks‡</th>
</tr>
</thead>
</table>
| Hormonal Implant                              | Placed under skin of arm by a clinician. Works for 3 years.¹ | >99%¹ | - Nothing to do or remember  
- Light or no periods  
- May decrease acne  
- No increased risk of clots | Irregular Periods |
| Hormonal IUD                                 | Placed in uterus by clinician. Self-check monthly. Works for 5 years.¹ | >99%¹ | - Light or no periods  
- No increased risk of clots | Irregular Periods |
| Non-Hormonal IUD                             | Placed in uterus by a clinician. Self-check monthly. Works for 10 years.³ | >99%³ | - No hormones  
- Periods remain regular  
- Effective immediately  
- No increased risk of clots | May cause heavier periods and cramping |
| Tubal Sterilization                          | Surgical procedure to close the tubes between the uterus and the ovaries. | >99%² | - It is a virtually permanent method of birth control  
- Nothing to do or remember | If you want to have child later, it is very difficult to re-open the tubes |
| Male Vasectomy                               | Surgical procedure that closes off the tubes that carry a partner’s sperm. | >99%² | - It is a virtually permanent method of birth control  
- Nothing to do or remember | If you want to have child later, it is very difficult to re-open the tubes |
| Hormonal Shot                                | Given every 3 months by a clinician. | >97%³ | - Light or no periods  
- No increased risk of clots | Irregular Periods  
May cause weight gain |
| Vaginal Ring                                 | You place in vagina. Replace monthly. | 92%¹ | - Lighter periods  
- May decrease acne | Blood clots |
| Hormonal Patch                               | You place on skin. Replace weekly. | 92%¹ | - Lighter periods  
- May decrease acne | Blood clots |
| Birth Control Pill (Combination Type)        | Swallow at the same time daily. | 92%¹ | - Lighter periods  
- May decrease acne | Blood clots |

<table>
<thead>
<tr>
<th>Secondary Method of Birth Control  (Choose One)</th>
<th>How to Use it</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condoms (with or without spermicide)</td>
<td>Partner must be willing to use each and every time you have sex.</td>
<td>Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS</td>
<td>Allergic Reactions</td>
</tr>
<tr>
<td>Cervical Cap, Diaphragm (must be used with spermicide). Vaginal Sponge</td>
<td>Place in vagina before you have sex.</td>
<td>You are in control of its use</td>
<td>Allergic Reactions</td>
</tr>
</tbody>
</table>

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.

†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.


Birth Control Methods That Are NOT Acceptable in The iPLEDGE® Program

You cannot use the following methods of birth control while you are taking isotretinoin. They do not give enough protection even when used with a second method of birth control.

- Birth control pills without estrogen (progesterone-only mini-pills)
- Female condoms
  - *A thin, loose-fitting, and flexible plastic tube that you put inside your vagina. It covers your cervix to block sperm.*
- Natural family planning (rhythm method or fertility awareness)
  - *This means not having sex during certain times of the month when you might be more likely to get pregnant. It does not work.*
- Breastfeeding
- Withdrawal
  - *Your partner can leak enough sperm to get you pregnant even if he does not ejaculate inside you.*
- Cervical shield*
  - *A silicone disc that sticks to your cervix to keep sperm out.*

*Web site: [www.ipledgeprogram.com](http://www.ipledgeprogram.com)
Phone system: 1-866-495-0654

*A cervical shield should not be confused with a cervical cap, which is an effective secondary method of contraception.*

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Making a Choice About Birth Control

General Advice

Your dermatologist, gynecologist, or family doctor will help you choose the right methods for you. They will also give you exact instructions on how to use them.

Choose methods that you will actually use all the time. This workbook will help you choose the 2 birth control methods that will be best for you.

Stay with your current primary method of birth control if:

- You are currently using an effective primary method AND you use it correctly. For example, you do not miss birth control pills or hormone shots.
- You are satisfied with your primary method.

Talk with your dermatologist, gynecologist, or family doctor about changing your birth control methods before you start isotretinoin treatment if you:

- Do not use your current method of birth control correctly. For example, you forget to change hormonal skin patches every week.
- Are not satisfied with the birth control method you are using now. Changing birth control methods in the middle of your isotretinoin treatment can be difficult.

You need to tell the doctor/prescriber who prescribes your isotretinoin if you decide to change methods of birth control during treatment. You may have to stop having sex until your new method of birth control is working. You may have to stop isotretinoin and wait until you have been using the new method with a second method for at least 1 month and have a negative pregnancy test.

What If I Cannot Use 2 Methods of Birth Control Together All The Time?

Talk with your dermatologist, gynecologist, or family doctor. If you plan to have sex during your treatment and feel you cannot be 100% successful in using 2 methods of birth control each time, you should not take isotretinoin.

What If My Birth Control Fails?

The section on “Emergency Birth Control (Emergency Contraception)” is on page 31 of this workbook. It tells you what emergency birth control is and where to get it quickly.
Planning Ahead If You Have a Partner

- Make sure your partner knows the facts about isotretinoin and birth defects. Show him the information on birth defects in this workbook. Your partner should understand the risks and benefits of isotretinoin.
- Make sure he knows you have to use 2 methods of birth control together correctly all the time for at least 1 month before beginning isotretinoin treatment, during treatment, and 1 month after the last dose of isotretinoin.

Primary Methods of Birth Control

This section of the workbook provides information about the different methods of primary birth control. It only gives you the most important information you need for the iPLEDGE® Program. It does not cover all the side effects or other information about these methods. If you want more information, ask your dermatologist, gynecologist, or family doctor.

None of the primary methods protect against sexually transmitted infections (STIs) or HIV/AIDS.

Hormonal Birth Control Methods

Hormonal birth control methods include birth control pills (combination type), skin patches, shots, under-the-skin implants, and the vaginal ring. They are prescription medicines that prevent pregnancy.

Hormonal Shots—Single Hormone

Hormonal shots use a progestin (a birth control hormone) to prevent pregnancy. They keep you from releasing eggs, keep eggs from growing in the uterus, and make it harder for sperm to get to an egg.

Who should not take single hormonal shots?

Some of the reasons you should not take single hormonal shots include:

- Unexplained vaginal bleeding
- History of or currently have breast cancer
- History of or currently have liver problems
- Pregnancy
How do I take single hormonal shots?
Your dermatologist, gynecologist, family doctor, or pharmacist (in some states) can give you a shot once every 12 weeks.

Are you taking single hormonal shots now?
If yes, is this going to be your primary method of birth control? How often do you miss shots?

Advantages
Some advantages may include:
- A single shot works for 12 weeks at a time
- There is no daily pill to take
- You can use it if you cannot take the hormone estrogen

Disadvantages
Some disadvantages may include:
- Single hormonal shots do not protect against STIs (sexually transmitted infections) or HIV/AIDS
- They may cause irregular bleeding
- If you are planning to get pregnant AFTER you finish your isotretinoin treatment, it may take up to 18 months to get pregnant after you stop getting single hormonal shots

How soon does the single hormonal shot start to work?
If you get the shot within the first 5 days of your menstrual flow, the protection against pregnancy begins right away.

Hormonal Intrauterine Device (IUD)
The hormonal IUD is a small piece of plastic your doctor/prescriber puts into your uterus. The hormonal IUD has a progestin (birth control hormone) that keeps you from releasing eggs and slows down sperm.

Who should not use a hormonal IUD?
Some of the reasons you should not use the hormonal IUD include:
- Conditions that may put you at risk for serious pelvic infection
- Unexplained vaginal bleeding
- Known or suspected cancer of the uterus, cervix, or breast
- Pregnancy
Hormonal Intrauterine Device (IUD) (Cont.)

How do I use a hormonal IUD?

Your gynecologist or family doctor can put in an IUD for you. It may cause cramping at first. The hormonal IUD can stay in place for up to 5 years.

Do you have a hormonal IUD now?

If you do, is this going to be your primary method of birth control? First, ask yourself these questions:

- Is the IUD in place?
- When did you last have it checked by your clinician? It needs to be checked within 3 months after you had it inserted.

Advantages

Some advantages may include:

- It is a good choice for long-term birth control (5 years)
- There is no daily pill to take
- It is a good choice if you are not at risk for STIs (sexually transmitted infections) and have not had a lot of pelvic infections

Disadvantages

Some disadvantages may include:

- An IUD does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- Side effects may include cramps and heavy and/or longer menstrual periods for the first few months after it is placed, and increased chance of infection

Hormonal Implants (Under-The-Skin)

Implantable birth control is a small plastic rod(s) (the size of a matchstick) which releases birth control hormones, that is put under the skin in the upper arm in the doctor’s/prescriber’s office. It is effective for up to 3 years but can be removed earlier.

Who should not use

Some of the reasons you should not use implantable birth control include:

- Unexplained vaginal bleeding
- History of or currently have breast cancer
- History of or currently have liver disease
- Pregnancy

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
How do I use a hormonal implant?

The implant is put under the skin by a healthcare provider in the doctor’s/prescriber’s office. It generally cannot be seen once under the skin and is effective for up to 3 years. It can be removed at any time by the healthcare provider.

Advantages

Some advantages may include:

- The plastic rod implant works for up to 3 years
- There is no daily pill to take

Disadvantages

Some disadvantages may include:

- Implant does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- May cause cramping or irregular bleeding
- There can be side effects related to putting in the implant and removing it. Discuss this with your doctor/prescriber.
- May be less effective in women who are overweight. Discuss this with your doctor/prescriber.
- Isotretinoin, antibiotics, and St. John’s Wort may make the implant less effective

How soon does the implant work?

Discuss this with your doctor/prescriber. Please make sure you can feel the implant rod under your skin after placement. If you cannot feel it, please do not start isotretinoin or have sexual intercourse until you talk to your doctor/prescriber.

Hormonal Birth Control Pills (Combination Type)

Hormonal birth control pills (combination type) are birth control pills you take by mouth every day as prescribed.

Who should not take birth control pills?

Some of the reasons you should not use birth control pills include:

- Smoking and you are over the age of 35
- History of or currently have blood clots
- History of or currently have breast cancer
- History of or currently have heart disease, liver problems, high blood pressure, or diabetes
- Pregnant or nursing
Hormonal Birth Control Pills (Cont.)

Why is it important how I take birth control pills?

Birth control pills provide very good protection only if you take them about the same time every day and do not miss any pills. If you miss pills, your chance of pregnancy is much greater. Your chance of getting pregnant is higher if you miss pills at the beginning of your cycle or start your pills too late in your cycle. Less than half of all females take their birth control pills as prescribed.

- The most important thing about using birth control pills as your primary method of birth control is taking them every day to keep the chance of pregnancy as low as possible. If you have not used them correctly, you may need to choose another primary method of birth control, such as the hormonal shot, an IUD, or a hormonal skin patch.
- Isotretinoin may make birth control pills less effective. That means you could be more likely to get pregnant while you are taking isotretinoin, particularly if you miss a pill.

Are you taking birth control pills now?

If you are, is this going to be your primary method of birth control? Before you decide, ask yourself:

- Do you ever have pills left at the end of the month?
- How often do you miss more than 1 pill per cycle? Do you do it more than 2 cycles in a year?
- Have you ever taken birth control pills out of order?

If you answered yes to any of these questions, you probably need to choose another primary method of birth control.

Progesterone-only birth control pills (mini-pills) are not acceptable for the iPLEDGE® Program because they are not an effective method of birth control. If you are using these, you will have to choose another primary method of birth control.

If you are not taking birth control pills now, why do you think you want to try them?

Ask yourself:

- Have you ever had to remember to take a pill every single day?
- Why do you think you can remember this task?

If you do not remember to take your pill every day without fail or have never taken pills every day before, you should probably choose a method of birth control other than birth control pills during isotretinoin treatment.
Advantages
Some advantages may include:
• Many patients have more regular, lighter, shorter, and less painful periods

Disadvantages
Some disadvantages may include:
• Birth control pills do not protect against STIs (sexually transmitted infections) or HIV/AIDS
• Common side effects include breakthrough bleeding, nausea and vomiting, and headaches
• If you skip pills, your chance of pregnancy is higher
• Isotretinoin, antibiotics, and St. John’s Wort may make birth control pills less effective

What should I do if I miss birth control pills when I am on isotretinoin?
• If you miss 1 pill, take it as soon as you remember. Continue taking your other pills at the regular time. Call your doctor/prescriber as soon as you realize it.
• If the whole day goes by before you realize you missed a pill, it is OK to take 2 pills together.
• If you miss more than 2 days, you should call your doctor/prescriber as soon as you realize it. You are at a greater chance for pregnancy if you start a cycle late or miss taking pills during the first week of each cycle.

Hormonal Skin Patch
The hormonal skin patch is a thin, plastic patch that you put on your skin. It releases birth control hormones into your body to protect against pregnancy.

Who should not use the hormonal skin patch?
Some of the reasons you should not use the patch include:
• Smoking and you are over the age of 35
• History of or currently have blood clots
• History of or currently have breast cancer
• History of or currently have heart disease, liver problems, high blood pressure, or diabetes
• Pregnancy or nursing
Hormonal Skin Patch (Cont.)

How do I use the hormonal skin patch?
You put on 1 patch which is worn for 1 week and replaced on the same day each week for 3 weeks. The fourth week is patch free, usually the time that you have a menstrual period. You place the hormonal skin patch where you can check it easily—on the upper outer arm, stomach, or upper body—but NOT on your breasts.

Are you using the hormonal skin patch now?
If you are, is this going to be your primary method of birth control? Before you decide, ask yourself:

- Do you have trouble remembering to change the patch each week? Has the patch ever come loose or fallen off and you did not immediately put on another one?
- Have you gained weight so that you weigh close to or more than 200 pounds?
If you answered yes to any of these questions, talk with your dermatologist, gynecologist, family doctor, or birth control counselor. Another primary method of birth control may be better for you.

Advantages
Some advantages may include:

- There is no daily pill to take
- Many patients have more regular, lighter, and shorter periods

Disadvantages
Some disadvantages may include:

- The patch does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- If it becomes loose or falls off for more than 24 hours, you can get pregnant
- If you leave the same patch on more than 1 week, you can get pregnant
- Common side effects include breakthrough bleeding, nausea and vomiting, headaches, and breast tenderness
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal methods less effective
- Possible increased risk of blood clots. Please discuss this with your doctor/prescriber.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Hormonal Vaginal Ring

The hormonal vaginal ring is a small flexible ring that you place into your vagina and change once a month. It releases birth control hormones into your body and works like birth control pills.

Who should not use the hormonal vaginal ring?

Some of the reasons you should not use the hormonal vaginal ring include:

- Smoking and you are over the age of 35
- History of or currently have blood clots
- History of or currently have breast cancer
- History of or currently have heart disease, liver problems, high blood pressure, or diabetes
- Pregnancy or nursing

How do I use the hormonal vaginal ring?

You put a new ring in your vagina once every 4 weeks on the same day of the week. You leave it there for 3 weeks and then take it out. During the 1-week break, you usually have a menstrual period. **If the ring slips out of the vagina during the 3-week period, you must replace it within 3 hours.**

Are you using the hormonal vaginal ring now?

If you are, is this going to be your primary method of birth control? Before you decide, ask yourself:

- Do you have trouble remembering to remove the ring after 3 weeks?
- Has the ring ever slipped out and you did not notice?
- Do you have trouble inserting the ring?

If you answered yes to any of these questions, talk with your dermatologist, gynecologist, family doctor, or birth control counselor. Another primary method of birth control may be better for you.
Hormonal Vaginal Ring (Cont.)

Advantages
Some advantages may include:

- There is no daily pill to take
- It does not need to be fitted by a doctor/prescriber
- Many female patients have more regular, lighter, and shorter menstrual periods

Disadvantages
Some disadvantages may include:

- The ring does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- You cannot use it with a diaphragm or cervical cap
- Some medicines for a vaginal yeast infection increase the level of hormones released into the blood
- You may have trouble inserting the ring
- Pregnancy can happen if:
  - The unopened package containing the ring is put into direct sunlight or exposed to very high temperatures
  - The ring slips out of the vagina and you do not replace it within 3 hours
  - The ring does not stay in the vagina for 3 weeks
  - You leave the ring in the vagina for more than 3 weeks
- Common side effects include breakthrough bleeding, nausea and vomiting, and headaches
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal methods less effective

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Non-hormonal Intrauterine Device (Copper IUD)

The copper IUD is a thin piece of plastic covered with the metal copper. It prevents pregnancy by slowing sperm down and keeping sperm from getting to the egg.

Who should not use the copper IUD?

Some of the reasons you should not use the copper IUD include:

- Conditions that may put you at risk for serious pelvic infection
- Unexplained vaginal bleeding
- Known or suspected cancer of the uterus, cervix, or breast
- Wilson’s disease (a rare inherited disorder that causes too much copper to accumulate in your liver, brain, and other vital organs)
- Pregnancy

How do I use the copper IUD?

Your gynecologist or family doctor can put in an IUD for you. It may cause cramping at first. The copper IUD can stay in place for up to 10 years.

Advantages

Some advantages may include:

- You can use it if you cannot take hormones
- It is a good choice for long-term birth control
- There is no daily pill to take

Disadvantages

Some disadvantages may include:

- An IUD does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- Side effects may include cramps, irregular bleeding, or heavy and longer menstrual periods

Web site: [www.ipledgeprogram.com](http://www.ipledgeprogram.com)
Phone system: 1-866-495-0654
Tubal Sterilization (Blocking Your Tubes)

Tubal sterilization (blocking your tubes) may be accomplished using a variety of surgical techniques that close the tubes between the uterus and the ovaries so that the sperm cannot get through to the egg. Tubal sterilization is considered to be very effective, virtually a permanent method of pregnancy prevention.

While an effective method of birth control, hysteroscopic tubal sterilization is not effective immediately and requires that a test be done at 3 months after the procedure to confirm that the tubes are blocked. For the purposes of the iPLEDGE® Program, hysteroscopic tubal sterilization is not considered an effective primary method of birth control unless the confirmation test has been performed.

Who should not have a tubal sterilization?

You should not have a tubal sterilization if you ever want to get pregnant, at any time now or in the future.

Advantages

Some advantages may include:

- It is a very effective and virtually permanent method of birth control
- There is no daily pill to take
- It works immediately after the surgery with the exception of hysteroscopic tubal sterilization

Disadvantages

Some disadvantages may include:

- Tubal sterilization does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- If you want to have a child later, it is very difficult to re-open the tubes
- It increases the chance of ectopic pregnancy (pregnancy in the tubes) if sperm manage to get through the blocked tubes
**Male Vasectomy**

A vasectomy is a surgical procedure that closes off the tubes that carry a partner’s sperm. If a man has sex before his doctor says his fluid has no sperm, the woman could get pregnant.

- If you have *only* 1 partner *and* he has had a vasectomy, this can be your primary method of birth control while taking isotretinoin. You must still use a second method of birth control.

**Advantages**

**Some advantages may include:**

- It is a very effective and virtually permanent method of birth control

**Disadvantages**

**Some disadvantages may include:**

- A vasectomy does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- If a male wants a child later, it is very difficult to open the tubes again
Secondary Methods of Birth Control

Secondary methods of birth control do not adequately protect against pregnancy if they are the only method used. However, they greatly increase your protection against getting pregnant if you use them along with a primary method every time you have sex. Effective secondary methods of birth control methods include barrier methods (male latex condoms, diaphragms, and cervical caps) and other methods (vaginal sponge). The diaphragm and cervical cap must always be used with a spermicide, and the male latex condom can be used with or without a spermicide. The vaginal sponge contains a spermicide. If a secondary method is your second method of birth control, you must use it every time you have sex. The female condom is not an effective secondary method for the iPLEDGE® Program.

Always use a spermicide with diaphragms and cervical caps.

Ask your doctor/prescriber, gynecologist, or family doctor to show you how to use secondary methods. Be sure you know how to use them correctly.

Make sure you know exactly how to use these methods of birth control. Know what mistakes people make with secondary methods. These mistakes can get you pregnant.

Spermicides

Spermicides come in several forms—creams, jellies, foams, or suppositories. You use a spermicide 10 to 30 minutes before you have sex—each and every time—whenever the male comes in or near the female’s vagina. Your dermatologist, gynecologist, family doctor, or birth control counselor can tell you how to use a spermicide with your secondary barrier method.

Some people are allergic to spermicides. If you cannot use a spermicide, you must use 2 primary methods of birth control together, or a primary method with a male latex condom as your second method.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
Male Latex Condom With or Without a Spermicide

The male latex condom, also called a “rubber,” is a thin cover put on the male’s penis that traps sperm. You can use a male latex condom with or without a spermicide.

Choosing a male latex condom as your secondary method

If you choose male latex condoms as a secondary method, your partner must be willing to use a male latex condom each and every time you have sex. Ask yourself:

• Does your sexual partner use a latex condom? Does he have a problem with using a latex condom each time you have sex?
• Have you and your partner ever forgotten to use latex condoms even when you had meant to?
• Have you ever had sex after drinking when you had not planned to?

Alcohol and drugs can affect your judgment and decisions about having sex.

Who should not use male latex condoms?

Some of the reasons your partner should not use male latex condoms (as your secondary method) include:

• You or your partner are allergic to latex
• Your partner does not want to use them
• You do not like to interrupt sex to let your partner put on a male latex condom
• You have had sex when you did not plan to and did not use birth control

You may want to choose a different method you can control and insert before having sex.

How does my partner use it?

The male latex condom is unrolled on a male’s erect penis before sex. Waiting too long lets sperm leak out.

You can use a male latex condom with or without a spermicide.

A male latex condom can only be used 1 time. Do not let your partner try to use it more than once. Safe lubricants include anything made with a water-based gel such as K-Y* Jelly.* Oils like petroleum jelly or baby oil can ruin a male latex condom.

Make sure the male latex condom stays on during sex. If it tears or comes off, call your doctor/prescriber about emergency birth control.

*K-Y® Jelly is a registered trademark of Reckitt Benckiser LLC.
Male Latex Condom With or Without a Spermicide (Cont.)

Advantages

Some advantages may include:

- It is effective immediately when put on correctly Male latex condoms do offer some protection against STIs (sexually transmitted infections) and HIV/AIDS
- You can usually tell when it breaks or slips off

Disadvantages

Some disadvantages may include:

- Your partner has to be committed to using male latex condoms. Some males do not like or want to use them. You are not in control of this birth control method.
- Male latex condoms can break or slip off during sex
- Males and females can have an allergy to latex

Diaphragm (Must Be Used With a Spermicide)

The diaphragm is a shallow latex cup edged with a flexible ring. It covers your cervix and keeps sperm from getting into your uterus. Your gynecologist or family doctor can fit you with one.

Choosing a diaphragm as your secondary method

Studies have shown that female patients under 30 and female patients who have sex 3 or more times a week have a higher pregnancy rate using diaphragms. If you are in 1 of these 2 groups, talk with your dermatologist, gynecologist, family doctor, or birth control counselor about whether the diaphragm is right for you.

- Do you find it easy to put in your diaphragm and remember to use it each time you have sex?
- Have you been using a spermicide with the diaphragm? You must use a spermicide with your diaphragm when in the iPLEDGE® Program.
- Have you had your diaphragm checked by your doctor/prescriber in the last 2 years to see if it still fits? You must have your diaphragm checked every 2 years, after a gain or loss of 10 pounds, or after childbirth or an abortion.
Who should not use the diaphragm?

Some of the reasons you should not use a diaphragm include:

- Allergy to latex or silicone
- Difficulty putting the diaphragm in and having it remain in place
- History of bladder infections or toxic shock
- Recent abortion

How do I use a diaphragm?

Before you insert the diaphragm, you put a spermicide in the center of the cup and around the ring. You bend the flexible ring and insert the diaphragm into your vagina. The back rim rests below and behind the cervix. The front rim is tucked behind your pubic bone.

You can put your diaphragm into the vagina up to 6 hours before sex. You have to leave it in place for at least 6 hours after you have sex. **You must put spermicide in the vagina each time you have sex again and leave the diaphragm in place for 6 hours after the last time.** You should not leave the diaphragm in for more than 24 hours at a time.

Advantages

Some advantages may include:

- It is effective immediately when put in correctly and used with a spermicide
- You can easily carry a diaphragm with you and you are in control of its use
- You do not have to interrupt sex play—it can be inserted before sex

Disadvantages

Some disadvantages may include:

- A diaphragm does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- You or your partner may have an allergy to latex
- Some females find it hard to insert
- It can get pushed out of place during sex
- You must check it for holes and tears and clean it after sex
Cervical Cap (Must Be Used With a Spermicide)

The cervical cap is a small cup that covers your cervix so that sperm cannot get in your uterus. You use it with a spermicide. It must fit perfectly to work. Your gynecologist or family doctor can fit you for one.

Choosing the cervical cap as your secondary method

Studies have shown that female patients under 30 and female patients who have sex 3 or more times a week have a higher pregnancy rate using the cervical cap. If you are in 1 of these 2 groups, talk with your gynecologist or family doctor about whether the cervical cap is right for you.

• Do you find it easy to put in your cervical cap and remember to use it each time you have sex?
• Have you been using spermicide with the cervical cap? You must use a spermicide with your cervical cap when in the iPLEDGE® Program

Who should not use a cervical cap?

Some of the reasons you should not use a cervical cap include:

• History of pelvic infections
• History of abnormal Pap tests
• History of Toxic Shock Syndrome (TSS)

How do I use a cervical cap?

The cap is filled one-third full with a spermicide. You squeeze it as you put it in your vagina. You press it onto the cervix to cover it completely. You can put the cap in the vagina right before sex, but it stays in place better if you put it in place 30 minutes before sex. You have to leave it in place for at least 6 hours after you have sex. You can leave in place up to 48 hours.

What is the difference between a diaphragm and a cervical cap?

The cervical cap is a little harder to learn how to use. With a cervical cap, there is no need to insert an extra spermicide if you have sex again. You can also leave the cap in place for a longer time—up to 48 hours. You cannot use the cervical cap if there is any vaginal bleeding, such as during your menstrual period.
Advantages

Some advantages may include:

• It is effective immediately when put in correctly and used with a spermicide
• You can easily carry a cervical cap with you and control its use
• It has no hormones
• There is no interruption of sex play—it can be inserted in advance

Disadvantages

Some disadvantages may include:

• A cervical cap does not protect against STIs (sexually transmitted infections) or HIV/AIDS
• You cannot use it during your menstrual period
• A cap lasts about 1 year
• You must check it for holes and tears and clean it after sex

Vaginal Sponge

The vaginal sponge is a soft foam disc containing 1 gram of the spermicide nonoxynol-9. Inserting the sponge puts spermicide in your vagina and keeps it there during sex. You insert it in the vagina before sex so it sits over your cervix. It has a string loop attached for easy removal.

Choosing the vaginal sponge as your secondary method

Have you ever used a vaginal sponge? What do you like or dislike about it?

• Do you find it easy to put in your vaginal sponge and remember to use it each time you have sex?
• Do you find it easy to take out?

Who should not use a vaginal sponge?

Female patients who are allergic to the spermicide nonoxynol-9 should not use the vaginal sponge.

How do I use the vaginal sponge?

First, wash your hands. Wet the sponge thoroughly with clean tap water. Squeeze the sponge gently several times until it is foamy. This releases the spermicide. Pinch the sides of the sponge together. Be sure the string loop is on the underside of the sponge. Squat or sit down, bend your wrist, and push the sponge gently up into your vagina as far as it will go. Check the position of the sponge to make sure the sponge covers your cervix.
**Vaginal Sponge (Cont.)**

**How do I take the sponge out?**

Wait at least 6 hours after the last time you had sex before taking the sponge out. You can leave it in place for up to 30 hours. You do not need more spermicide if you have sex more than once during that time. To take the sponge out, you need to catch the string loop and gently pull on it.

**Advantages**

**Some advantages may include:**

- It is effective immediately
- You can easily carry a vaginal sponge with you and control its use
- It has no hormones
- There is no interruption of sex play—it can be inserted in advance and is effective for up to 30 hours

**Disadvantages**

**Some disadvantages may include:**

- The vaginal sponge does not protect against STIs (sexually transmitted infections) or HIV/AIDS
- It is not as effective in female patients who have had children
Emergency Birth Control (Emergency Contraception)

Emergency birth control is meant only for emergencies. It does NOT take the place of your usual 2 methods of birth control and it will not protect against sexually transmitted infections (STIs). Emergency birth control is not to be used instead of regular birth control and it does not work if you are already pregnant.

Emergency birth control is also called “after sex” or “morning after” birth control. It can prevent pregnancy after sex without adequate protection. Emergency birth control prevents release of the egg, joining of the sperm and the egg, or implanting of the egg in the uterus. Emergency birth control is only for a female patient who is sure she is not already pregnant.

There are 2 methods of emergency birth control:

1. Emergency Contraceptive Pills (ECPs)—some must be used within 3 days, others must be used within 5 days of having sex without adequate protection. The sooner you take ECPs, the more likely they are to work. It is best if ECPs are started within 12 hours after you have sex without adequate protection. The pills may give you severe nausea. Ask your doctor/prescriber for something to help with the nausea if you need this treatment. ECPs do not take the place of your usual birth control, nor do they continue to prevent pregnancy during the rest of your menstrual cycle.

2. Copper IUD—you need to have the IUD inserted within 5 days of having sex without adequate protection.

When would I need emergency birth control?

Call your doctor/prescriber or gynecologist about emergency birth control if you had sex without adequate protection, such as:

- You forgot to take 2 or more birth control pills and had sex
- You had sex without using a second method of birth control
- You were late for your birth control hormonal shot and had sex
- Your partner’s condom broke or slipped off
- Your diaphragm or cervical cap slipped out of place or ripped during sex
Emergency Birth Control (Cont.)

Where can I get emergency birth control?

You can get emergency birth control from:

- Private doctors or nurse practitioners
- Planned Parenthood
- Women’s health centers
- Many hospital emergency rooms (unless they are owned by organizations opposing birth control)
- Available over-the-counter

Reasons Female Patients Get Pregnant

Some of the reasons female patients get pregnant:

- After they committed to be abstinent in the iPLEDGE® Program they did not avoid sex with a male
- They did not use 2 methods of birth control all the time and every time they had sex
- They did not use 2 methods of birth control the right way
- One method of birth control failed

It is very important that you use your 2 methods of birth control all the time and every time you have sex. If 2 methods of birth control are used every time properly, as the iPLEDGE Program requires, your chances of getting pregnant are very small.

Sex, Alcohol, and Drugs

Alcohol and drugs can make you unable to use good judgment. You must remember to use 2 effective methods of birth control together each and every time you have sex with a male for 1 month before you start taking isotretinoin, during, and for 1 month after stopping treatment. Remember to make good decisions to ensure you use your secondary method the right way.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Recognizing Pregnancy

If you think you might be pregnant, stop isotretinoin and call your doctor/prescriber right away. Here are some signs and symptoms that you might be pregnant:

- You miss your menstrual period
- You have nausea (generally first thing in the morning)
- Your breasts feel really tender, like at the beginning of a menstrual period
- The area around your nipples may look darker
- You feel really tired and want to sleep
- You feel you have to go to the bathroom a lot
- You may have spotting of blood at the time of your menstrual period, but no real bleeding

Ectopic (Tubal) Pregnancy

Sometimes a baby starts to grow outside the uterus. This is a serious problem. Call your doctor/prescriber right away, if you have these signs:

- Sudden pain or severe cramping in your lower abdomen
- Bleeding or spotting with abdominal pain after you miss a menstrual period
- Fainting or dizziness lasting more than a few seconds
**WARNING**
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

**IMPORTANT NOTICE**
Use only isotretinoin products approved by the US Food and Drug Administration.

Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Guide to Isotretinoin
For Female Patients
Who Can Get Pregnant

The importance of avoiding pregnancy on isotretinoin

The tools you need to help you prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment

- Patient ID Cards and Informed Consent forms located inside back cover pocket

WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.
Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

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CAUSES
BIRTH DEFECTS
DO NOT GET PREGNANT
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guide to Isotretinoin for Female Patients Who Can Get Pregnant</td>
<td>4</td>
</tr>
<tr>
<td>Effective Methods of Birth Control</td>
<td>7</td>
</tr>
<tr>
<td>iPLEDGE® Program Checklist</td>
<td>12</td>
</tr>
<tr>
<td>Patient Information/Informed Consent Forms (for all patients)</td>
<td>15*</td>
</tr>
<tr>
<td>Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)</td>
<td>15*</td>
</tr>
<tr>
<td>Patient Identification Cards</td>
<td>15*</td>
</tr>
</tbody>
</table>

*Located inside back cover pocket.
What Is Isotretinoin?

Isotretinoin (eye-soh-tret-in-OH-in) is a prescription medication that treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months. Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby’s mother takes isotretinoin. You should also learn about the side effects and the precautions and warnings (see the enclosed sheet entitled Safety Information About Isotretinoin).

What Is The iPLEDGE® Program?

To avoid serious risks to unborn babies, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for isotretinoin. The iPLEDGE Program is a single, shared (includes multiple manufacturers) system with requirements for prescribers, pharmacies, and patients. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to
- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Only registered and activated prescribers can prescribe isotretinoin and only registered and activated pharmacies can dispense isotretinoin. In order to receive isotretinoin, all patients must be enrolled in the iPLEDGE Program and agree to follow the requirements.
What Do All Patients Need To Know?

Prevent Pregnancy and Birth Defects
There is a very high chance that babies born to female patients taking isotretinoin will be deformed, born too early, or die before they are born. This can happen even if a female patient takes isotretinoin for only a short time. It may also happen if a pregnant female receives a blood transfusion from someone taking isotretinoin.

Do male patients taking isotretinoin need to worry about birth defects?
Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin.

If you are worried about isotretinoin birth defects from sperm, you can use a male latex condom to help prevent pregnancy. Use a condom each and every time you have intercourse (sex) while you are taking isotretinoin and for 1 month after you stop taking it.

Can isotretinoin affect a male patient’s ability to father healthy children?
Studies on isotretinoin did not show effects on sperm count, how sperm look, or how well they swim and move.

Do Not Donate Blood
Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant female gets blood from you. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone
You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

Obtain Your Prescription
Obtain your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

The web site, www.ipledgeprogram.com, has a list of registered pharmacies. Once on the web site choose “Find a Participating Pharmacy” in the left navigation. A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.
What Do Female Patients Who Can Get Pregnant Need To Know?

DO NOT take isotretinoin if you are pregnant.
DO NOT get pregnant before starting isotretinoin, while taking it, and for 1 month after your last dose.

Before you can begin isotretinoin treatment, there is a 30-day wait period where you must be on 2 methods of birth control. Additionally, you need to have 2 negative pregnancy tests. They can be urine or blood tests. You will need to plan with your doctor/prescriber when and where to take your pregnancy tests.

- You take the first test when you decide to take isotretinoin.
- You take the second test during the first 5 days of the menstrual period right before you start isotretinoin. This pregnancy test must be done by an approved lab. The interval between the 2 tests must be at least 19 days.

You must take a pregnancy test every month done by an approved lab during treatment. You also take a pregnancy test after your last dose, and 1 month after your last dose. You will need to plan with your doctor/prescriber when to take your pregnancy test each month.

Have 2 negative pregnancy tests before you start isotretinoin.

Have a negative pregnancy test before you obtain each monthly prescription.

To keep from getting pregnant, you need to use 2 effective methods of birth control together correctly all the time:

- For at least 1 month before you start isotretinoin
- During treatment which usually lasts 4 to 5 months
- For 1 month after your last dose—to continue protection against pregnancy

Any method of birth control can fail. Using 2 methods of birth control together all the time drastically reduces the chance that you will get pregnant.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
### Primary Method of Birth Control (Choose One)*

<table>
<thead>
<tr>
<th>Method</th>
<th>How to Use it</th>
<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonal Implant</td>
<td>Placed under skin of arm by a clinician. Works for 3 years.¹</td>
<td>&gt;99%¹</td>
<td>• Nothing to do or remember&lt;br&gt;• Light or no periods&lt;br&gt;• May decrease acne&lt;br&gt;• No increased risk of clots</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td>Hormonal IUD</td>
<td>Placed in uterus by clinician. Self-check monthly. Works for 5 years.¹</td>
<td>&gt;99%¹</td>
<td>• Light or no periods&lt;br&gt;• No increased risk of clots</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td>Non-Hormonal IUD</td>
<td>Placed in uterus by a clinician. Self-check monthly. Works for 10 years.³</td>
<td>&gt;99%³</td>
<td>• No hormones&lt;br&gt;• Periods remain regular&lt;br&gt;• Effective immediately&lt;br&gt;• No increased risk of clots</td>
<td>May cause heavier periods and cramping</td>
</tr>
<tr>
<td>Tubal Sterilization</td>
<td>Surgical procedure to close the tubes between the uterus and the ovaries.</td>
<td>&gt;99%²</td>
<td>• It is a virtually permanent method of birth control&lt;br&gt;• Nothing to do or remember</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
</tr>
<tr>
<td>Male Vasectomy</td>
<td>Surgical procedure that closes off the tubes that carry a partner’s sperm.</td>
<td>&gt;99%³</td>
<td>• It is a virtually permanent method of birth control&lt;br&gt;• Nothing to do or remember</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
</tr>
<tr>
<td>Hormonal Shot</td>
<td>Given every 3 months by a clinician.</td>
<td>&gt;97%¹</td>
<td>• Light or no periods&lt;br&gt;• No increased risk of clots</td>
<td>Irregular Periods&lt;br&gt;May cause weight gain</td>
</tr>
<tr>
<td>Vaginal Ring</td>
<td>You place in vagina. Replace monthly.</td>
<td>92%¹</td>
<td>• Lighter periods&lt;br&gt;• May decrease acne</td>
<td>Blood clots</td>
</tr>
<tr>
<td>Hormonal Patch</td>
<td>You place on skin. Replace weekly.</td>
<td>92%¹</td>
<td>• Lighter periods&lt;br&gt;• May decrease acne</td>
<td>Blood clots</td>
</tr>
<tr>
<td>Birth Control Pill (Combination Type)</td>
<td>Swallow at the same time daily.</td>
<td>92%¹</td>
<td>• Lighter periods&lt;br&gt;• May decrease acne</td>
<td>Blood clots</td>
</tr>
</tbody>
</table>

### Secondary Method of Birth Control (Choose One)

<table>
<thead>
<tr>
<th>Method</th>
<th>How to Use it</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condoms (with or without spermicide)</td>
<td>Partner must be willing to use each and every time you have sex.</td>
<td>Protec</td>
<td>Allergic Reactions</td>
</tr>
<tr>
<td>Cervical Cap, Diaphragm (must be used with spermicide).</td>
<td>Place in vagina before you have sex.</td>
<td>You are in control of its use</td>
<td>Allergic Reactions</td>
</tr>
<tr>
<td>Vaginal Sponge</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.

†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.


Reasons you would not have to use 2 methods of birth control

There are 2 reasons you would not have to use 2 effective methods of birth control.

- You commit to abstinence which means not having sex or sexual contact with any male 24 hours a day, 7 days a week for 1 month before, during, and for 1 month after your isotretinoin treatment.

- You are unable to get pregnant because:
  - You have entered menopause, and your doctor/prescriber has confirmed this
  - You do not have either of your 2 ovaries and/or a uterus, and your doctor/prescriber has confirmed this

If you have any questions about being able to get pregnant, talk with your doctor/prescriber.

You can only obtain your prescription for isotretinoin if:

- Your pregnancy test was negative
- Your doctor/prescriber entered your 2 methods of birth control in the iPLEDGE® Program system
- You answered your comprehension questions in the iPLEDGE Program system correctly. These questions will demonstrate your understanding of the iPLEDGE Program requirements, the birth control that you have chosen, and the risks associated with isotretinoin. Note: you can answer your comprehension questions only after your doctor/prescriber has entered your pregnancy test result and confirmed your monthly office visit in the iPLEDGE Program system. You will need your patient ID number to answer your comprehension questions on the iPLEDGE Program web site or by calling 1-866-495-0654
- You also entered your 2 methods of birth control and they match the birth control options entered by your doctor/prescriber

Please read the iPLEDGE Program Birth Control Information Sheet and for additional information on birth control options read the enclosed Birth Control Workbook.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
The iPLEDGE Program Pregnancy Registry

Because isotretinoin causes such severe birth defects, it is very important for us to know about all the pregnancies that happen during treatment and within 1 month after the last dose. If you think you are pregnant call your doctor/prescriber. The confidential iPLEDGE Program Pregnancy Registry is a way to collect that information. It may help us prevent more pregnancies in the future.

Your doctor/prescriber will tell you about the confidential iPLEDGE Program Pregnancy Registry. You are encouraged to contact the iPLEDGE Program Pregnancy Registry at 1-800-681-7247 if you get pregnant.

Obtaining Your Prescription

You obtain the prescription within the 7-day prescription window (1 week) of the date of your pregnancy test, counting the date of the pregnancy test as DAY 1.

The iPLEDGE Program system will automatically compute the “Do Not Dispense To Patient After” date for your pharmacist.

To figure out the last date you can obtain your prescription, add 6 to the date of your pregnancy test. For example:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2 – Day 6</th>
<th>Day 7 – Last day to obtain prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day of the pregnancy test</strong> (Friday, March 1)</td>
<td><strong>(Saturday, March 2 thru Wednesday, March 6)</strong></td>
<td><em>(Thursday, March 7)</em></td>
</tr>
</tbody>
</table>

The 7-day prescription window expires at 11:59 p.m. Eastern Time on Day 7 of the prescription window. Your pharmacist will not be able to fill your prescription after this time. If your 7-day prescription window expires before you obtain your prescription, you can start a new 7-day prescription window right away (unless it is your first prescription window), but you must repeat the program requirements to get another prescription. Additional information regarding the specific dates of your 7-day prescription window, and other information about your current status can be found by selecting “My Program Status” on the web site from the Patient home page (after you log in).

**Note:** Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.
Talk With an Expert

If you want to talk to a birth control expert, such as a gynecologist or family
doctor/prescriber, about your birth control, the doctor/prescriber who prescribes
isotretinoin for you can refer you. The makers of isotretinoin will pay for this
referred visit. Take the \textit{Contraception Counseling Guide And Contraception
Referral Form} with you.

Changing Your Birth Control

Tell the doctor/prescriber who prescribes your isotretinoin if you need to change your birth
control during your isotretinoin treatment. Depending on the type of birth control you change
to, you may have to \textit{stop} isotretinoin and wait until you have been on the new birth control for
at least 1 month and have a negative pregnancy test.

Changing From Abstinence

If you have chosen abstinence (not having sex or sexual contact with any male) and you
decide to start having sexual activity, you must tell the doctor/prescriber who prescribes your
isotretinoin before you engage in sexual activity. Before you continue isotretinoin, you and
your doctor/prescriber must make a plan to start your birth control and be sure you are
not pregnant.

\textbf{One of the most common reasons that women get pregnant is that they do not avoid sexual activity when they plan to be abstinent.}

Video: \textit{Be Prepared, Be Protected, and Be Aware: The Risk Of Pregnancy While On Isotretinoin}

Your doctor/prescriber has a video that shows the kinds of birth defects that may happen if a
woman takes any amount of isotretinoin while she is pregnant. It also reviews the steps for
preventing pregnancy.
Changing to a New Doctor/Prescriber

You can change your doctor/prescriber through the iPLEDGE Program web site, www.ipledgeprogram.com, by choosing “Change Primary Prescriber” from the menu or by calling 1-866-495-0654. Once you make the change, you will not be able to get any more prescriptions from your original doctor/prescriber.

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.
BEFORE TREATMENT

PLANNING

☐ Talk with your doctor/prescriber about isotretinoin and the iPLEDGE Program
☐ Sign the Patient Information/Informed Consent (for all patients) form
☐ Sign the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
☐ Have your first urine or blood pregnancy test, which can be performed at the doctor’s/prescriber’s office
☐ Registration—ensure your doctor/prescriber registers you in the iPLEDGE Program. You must be registered for at least 30 days prior to your first prescription.
☐ Get your patient ID card containing your patient ID number from your doctor/prescriber. Keep your patient ID number in a safe place.
☐ Receive your password in the mail

BIRTH CONTROL

☐ Read the iPLEDGE Program Birth Control Information Sheet and for additional information on birth control options read the Birth Control Workbook
☐ Talk with your dermatologist, gynecologist, family doctor, or a birth control expert about effective birth control options
☐ Choose 2 effective methods of birth control
☐ Start using the 2 methods of birth control together for at least 1 month before you start isotretinoin

YOUR FIRST PRESCRIPTION

☐ Have a second pregnancy test conducted at an approved lab within the first 5 days of your menstrual period (at least 30 days after registration)
☐ Answer questions about the iPLEDGE Program and confirm your 2 methods of birth control
  • Note: you can answer your comprehension questions only after your doctor/prescriber has entered your pregnancy test result in the iPLEDGE Program system
☐ Obtain your prescription for up to a maximum of a 30-day supply
  • Note: isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack and provide fewer than 10 capsules.
☐ Obtain your prescription within the 7-day prescription window, counting the date of the pregnancy test as DAY 1
  • If you do not obtain your prescription within the 7-day prescription window, you will need to go back to your doctor/prescriber to start this process again
☐ Use 2 effective methods of birth control together all the time
☐ Keep your appointments every month to get a prescription
☐ See your doctor/prescriber for a monthly pregnancy test
☐ Answer different questions each month about the iPLEDGE Program

DURING TREATMENT

☐ Use 2 effective methods of birth control together all the time
☐ See your doctor/prescriber for a monthly pregnancy test
☐ Keep your appointments every month to get a prescription
☐ Confirm your 2 methods of birth control by entering them into the iPLEDGE Program system
☐ Answer different questions each month about the iPLEDGE Program
  • Note: you can answer your comprehension questions only after your doctor/prescriber has entered your pregnancy test result in the iPLEDGE Program system
☐ Obtain your prescription for up to a maximum of a 30-day supply
☐ Obtain your prescription within the 7-day prescription window counting the day of the pregnancy test as DAY 1
  • If you do not obtain your prescription within the 7-day prescription window, you will need to go back to your doctor/prescriber to start this process again
☐ Do not donate blood

AFTER TREATMENT

RIGHT AFTER YOUR LAST DOSE

☐ Get a pregnancy test after your last dose
☐ Confirm that your doctor/prescriber has entered the results of this pregnancy test into the iPLEDGE Program system
☐ Continue using your 2 methods of birth control for 1 month
☐ Do not share any leftover isotretinoin with anyone
☐ Do not donate blood for 1 month after your last dose

ONE MONTH AFTER YOUR LAST DOSE

☐ Have a final pregnancy test at 1 month after your last dose
☐ Confirm that your doctor/prescriber has entered the results of this pregnancy test into the iPLEDGE Program system

Reference ID: 4252185
**Patient Information/Informed Consent**

**Informed Consent About Birth Defects**

Important forms you must sign before you begin taking isotretinoin.

**Patient Identification Cards**

Remove one ID card and take it along with your prescription to the pharmacy (within your prescription window) to obtain your isotretinoin. Separate the cards and keep the duplicate ID card in a safe place.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Patient Information/Informed Consent
(for all patients):
To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.
Read each item below and initial in the space provided if you understand each item and agree to follow your doctor’s instructions. A parent or guardian of a patient under age 18 must also read and understand each item before signing the agreement.
Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I, _____________________________  
   (Patient’s Name)  
   understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.  
   Initials: ______

2. My doctor has told me about my choices for treating my acne.  
   Initials: ______

3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. (Note: There is a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)).  
   Initials: ______

4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, “anxious” or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have had thoughts about hurting themselves or taking their own life (suicidal thoughts).  
   Initials: ______

5. Before I start taking isotretinoin, I agree to tell my doctor if I have ever had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.  
   Initials: ______

6. Before I start taking isotretinoin, I agree to tell my doctor if, to the best of my knowledge, anyone in my family has ever had symptoms of depression, been psychotic, attempted suicide, or had any other serious mental problems.  
   Initials: ______

7. Once I start taking isotretinoin, I agree to stop using isotretinoin and tell my doctor right away if any of the following signs and symptoms of depression or psychosis happen:  
   • Start to feel sad or have crying spells  
   • Lose interest in activities I once enjoyed  
   • Sleep too much or have trouble sleeping  
   • Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)  
   • Have a change in my appetite or body weight  
   • Have trouble concentrating  
   • Withdraw from my friends or family  
   • Feel like I have no energy  
   • Have feelings of worthlessness or guilt  
   • Start having thoughts about hurting myself or taking my own life (suicidal thoughts)  
   • Start acting on dangerous impulses  
   • Start seeing or hearing things that are not real  
   Initials: ______

8. I agree to return to see my doctor every month I take isotretinoin to get a new prescription for isotretinoin, to check my progress, and to check for signs of side effects.  
   Initials: ______

9. Isotretinoin will be prescribed just for me — I will not share isotretinoin with other people because it may cause serious side effects, including birth defects.  
   Initials: ______

10. I will not give blood while taking isotretinoin or for 1 month after I stop taking isotretinoin. I understand that if someone who is pregnant gets my donated blood, her baby may be exposed to isotretinoin and may be born with serious birth defects.  
    Initials: ______

11. I have read the Patient Introductory Brochure and other materials my provider provided me containing important safety information about isotretinoin. I understand all the information I received.  
    Initials: ______

12. My doctor and I have decided I should take isotretinoin. I understand that I must be qualified in the iPLEDGE Program to have my prescription filled each month. I understand that I can stop taking isotretinoin at any time. I agree to tell my doctor if I stop taking isotretinoin.  
    Initials: ______

I now allow my doctor ___________________________ to begin my treatment with isotretinoin.

Patient Signature: ___________________________ Date: _____________

Parent/Guardian Signature (if under age 18): ___________________________ Date: _____________

Patient Address ___________________________ Telephone – – – – –

Patient Name (print) ___________________________

I have:  
• fully explained to the patient, ___________________________, the nature and purpose of isotretinoin treatment, including its benefits and risks  
• provided the patient the appropriate educational materials, such as the Patient Introductory Brochure and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin  
• answered those questions to the best of my ability

Doctor Signature: ___________________________ Date: _____________

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT’S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.

www.implegprogram.com | 1-866-495-0654
Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)

To be completed by the patient (and her parent or guardian* if patient is under age 18) and signed by her doctor.

Read each item below and initial in the space provided to show that you understand each item and agree to follow your doctor’s instructions. Do not sign this consent and do not take isotretinoin if there is anything that you do not understand.

* A parent or guardian of a minor patient (under age 18) must also read and initial each item before signing the consent.

(Patient’s Name)

1. I understand that there is a very high chance that my unborn baby could have severe birth defects if I am pregnant or become pregnant while taking isotretinoin. This can happen with any amount and even if taken for short periods of time. This is why I must not be pregnant while taking isotretinoin.

   Initial: ______

2. I understand that I must not get pregnant one month before, during the entire time of my treatment, and for one month after the end of my treatment with isotretinoin.

   Initial: ______

3. I understand that I must avoid sexual intercourse completely, or I must use two separate, effective methods of birth control (contraception) at the same time. The only exceptions are if I have had surgery to remove the uterus (a hysterectomy) or both of my ovaries (bilateral oophorectomy), or my doctor has medically confirmed that I am post-menopausal.

   Initial: ______

4. I understand that hormonal birth control products are among the most effective methods of birth control. Combination birth control pills and other hormonal products include skin patches, shots, under-the-skin implants, vaginal rings, and intrauterine devices (IUDs). Any method of birth control can fail. That is why I must use two different birth control methods at the same time, starting one month before, during, and for one month after stopping therapy every time I have sexual intercourse, even if one of the methods I choose is hormonal birth control.

   Initial: ______

5. I understand that the following are effective methods of birth control:

   Primary methods
   • tying my tubes (tubal sterilization)
   • male vasectomy
   • intrauterine device
   • hormonal (combination birth control pills, skin patches, shots, under-the-skin implants, vaginal rings, or vaginal ring)

   Secondary methods
   Barrier: male latex condom with or without spermicide
diaphragm with spermicide
cervical cap with spermicide
Ober: vaginal sponge (contains spermicide)

A diaphragm and cervical cap must each be used with spermicide, a special cream that kills sperm

I understand that at least one of my two methods of birth control must be a primary method.

Initial: ______

6. I will talk with my doctor about any medicines including herbal products I plan to take during my isotretinoin treatment because hormonal birth control methods may not work if I am taking certain medicines or herbal products.

Initial: ______

7. I may receive a free birth control counseling session from a doctor or other family planning expert. My isotretinoin doctor can give me an Isotretinoin Contraception Referral Form for this free consultation.

Initial: ______

My doctor has answered all my questions about isotretinoin and I understand that it is my responsibility not to get pregnant one month before, during isotretinoin treatment, or for one month after I stop taking isotretinoin.

Initial: ______

I now authorize my doctor to begin my treatment with isotretinoin.

Patient Signature: ___________________________ Date: ___________________________

Parent/Guardian Signature (if under age 18): ___________________________ Date: ___________________________

Please print: Patient Name and Address: ___________________________ Telephone: ___________________________

I have fully explained to the patient, ___________________________, the nature and purpose of the treatment described above and the risks to females of reproductive potential. I have asked the patient if she has any questions regarding her treatment with isotretinoin and have answered those questions to the best of my ability.

Doctor Signature: ___________________________ Date: ___________________________

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT’S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.
• Visit your doctor/prescriber monthly
• Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
• Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
• Do not get pregnant
• Do not share your drug
• Do not donate blood

See reverse for important safety information

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

Duplicate ID Card

• Visit your doctor/prescriber monthly
• Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
• Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
• Do not get pregnant
• Do not share your drug
• Do not donate blood

See reverse for important safety information

Peel off sticker for patient’s file

Patient ID number
WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.
Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Peel off sticker for patient’s file

Duplicate ID Card

• Visit your doctor monthly
• Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
• Take this card and your prescription to the pharmacy within the prescription window to obtain your prescription
• Do not get pregnant
• Do not share your drug
• Do not donate blood

Stop isotretinoin and call your doctor right away if you are pregnant.
Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

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See reverse for important safety information

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Reference ID: 4252185
The iPLEDGE Program

Contraception Counseling
Guide And Contraception
Referral Form

Referral form for contraception counseling
and guide for counselors to effective methods
of contraception

WARNING
Isotretinoin must not be used by female patients who are or may
become pregnant. There is an extremely high risk that severe birth
defects will result if pregnancy occurs while taking isotretinoin in any
amount, even for a short period of time. Potentially any fetus exposed
during pregnancy can be affected. There are no accurate means of
determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.
Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

**TABLE OF CONTENTS**

- Contraception counseling for isotretinoin patients ........................................... 3
- Counseling goals ................................................................................................. 6
- Contraception requirements .............................................................................. 7
- Unacceptable methods of contraception ............................................................. 9
- Emergency contraception ................................................................................. 9
- Abstinence ............................................................................................................ 9
- Reporting a pregnancy ....................................................................................... 10
- Contraception referral form .............................................................................. 11*
- Reimbursement referral form ............................................................................. 11*

*Located inside back cover pocket.
Contraception Counseling For Isotretinoin Patients

Isotretinoin is used to treat severe recalcitrant nodular acne; however, it is also a known human teratogen. Over one third of all babies exposed to isotretinoin in utero and carried to term have major birth defects.¹,²

What Is The iPLEDGE® Program?

To avoid serious risks to unborn babies, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for isotretinoin. The iPLEDGE Program is a single, shared (includes multiple manufacturers) system with requirements for prescribers, pharmacies, and patients. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to

- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

Only registered and activated prescribers can prescribe isotretinoin and only registered and activated pharmacies can dispense isotretinoin. In order to receive isotretinoin, all patients must be enrolled in the iPLEDGE Program and agree to follow the requirements.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654
Your Role

This patient is being referred to you because she has asked for counseling to help her decide which contraceptive methods are best for her and that will enable her to comply with the contraception requirements of the iPLEDGE® Program.

The patient must select and commit to using 2 methods of effective contraception simultaneously, at least 1 of which must be a primary method, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. She must use 2 methods of effective contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment.

Isotretinoin is not recommended for sexually active females of reproductive potential whom you believe will not be able to maintain abstinence or will not use contraception, as the program requires.

Please read this Contraception Counseling Guide And Contraception Referral Form completely before you begin your counseling session. These provide an overview of the counseling goals for the patient and the contraception requirements of the iPLEDGE Program. They do not contain detailed information on the various methods of contraception.

The Birth Control Workbook, which is for patients, contains more information on effective primary and secondary methods of contraception. It is not complete information on any of the methods, and the patient is encouraged to ask questions about specific methods or issues. Additionally, the patient received an iPLEDGE Program Birth Control Information Sheet which lists the approved primary and secondary methods of birth control required for the iPLEDGE Program (www.ipledgeprogram.com).
# Program Approved Methods of Contraception

Choose 1 Primary + 1 Secondary Birth Control Method

<table>
<thead>
<tr>
<th>Primary Method of Birth Control (Choose One)*</th>
<th>How to Use it</th>
<th>How Well it Works</th>
<th>Benefits†</th>
<th>Risks‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonal Implant</td>
<td>Placed under skin of arm by a clinician. Works for 3 years.¹</td>
<td>&gt;99%¹</td>
<td>• Nothing to do or remember</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td>Hormonal IUD</td>
<td>Placed in uterus by clinician. Self-check monthly. Works for 5 years.¹</td>
<td>&gt;99%¹</td>
<td>• Light or no periods</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td>Non-Hormonal IUD</td>
<td>Placed in uterus by a clinician. Self-check monthly. Works for 10 years.³</td>
<td>&gt;99%³</td>
<td>• No hormones</td>
<td>May cause heavier periods and cramping</td>
</tr>
<tr>
<td>Tubal Sterilization</td>
<td>Surgical procedure to close the tubes between the uterus and the ovaries.</td>
<td>&gt;99%²</td>
<td>• It is a virtually permanent method of birth control</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
</tr>
<tr>
<td>Male Vasectomy</td>
<td>Surgical procedure that closes off the tubes that carry a partner's sperm.</td>
<td>&gt;99%²</td>
<td>• It is a virtually permanent method of birth control</td>
<td>If you want to have child later, it is very difficult to re-open the tubes</td>
</tr>
<tr>
<td>Hormonal Shot</td>
<td>Given every 3 months by a clinician.</td>
<td>&gt;97%¹</td>
<td>• Light or no periods</td>
<td>Irregular Periods</td>
</tr>
<tr>
<td>Vaginal Ring</td>
<td>You place in vagina. Replace monthly.</td>
<td>92%¹</td>
<td>• Lighter periods</td>
<td>Blood clots</td>
</tr>
<tr>
<td>Hormonal Patch</td>
<td>You place on skin. Replace weekly.</td>
<td>92%¹</td>
<td>• Lighter periods</td>
<td>Blood clots</td>
</tr>
<tr>
<td>Birth Control Pill (Combination Type)</td>
<td>Swallow at the same time daily.</td>
<td>92%¹</td>
<td>• Lighter periods</td>
<td>Blood clots</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Method of Birth Control (Choose One)</th>
<th>How to Use it</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condoms (with or without spermicide)</td>
<td>Partner must be willing to use each and every time you have sex.</td>
<td>• Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS</td>
<td>Allergic Reactions</td>
</tr>
<tr>
<td>Cervical Cap, Diaphragm (must be used with spermicide). Vaginal Sponge</td>
<td>Place in vagina before you have sex.</td>
<td>• You are in control of its use</td>
<td>Allergic Reactions</td>
</tr>
</tbody>
</table>

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.

†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.


Counseling Goals
Ensure That The Patient:

• Understands and commits fully to not becoming pregnant
• Commits to using 2 methods of contraception together simultaneously, consistently, and correctly. She must use 2 methods of effective contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment
• Chooses the methods of contraception that will work best for her and that she and her partner will actually use
• If, after counseling, the patient recognizes she will not be able to commit fully to the iPledge Program contraception requirements, encourage her to not take isotretinoin and do not prescribe or if counseling, inform her prescriber
• Commits fully to abstinence (not having sex or sexual contact with any male 24 hours a day, 7 days a week) for 1 month before, during, and for 1 month after she stops taking isotretinoin
• Knows when to contact her prescriber for emergency contraception
• Understands the risk of having a child with significant birth defects from exposure to isotretinoin

Counseling Younger Teens

For younger teens, it is important to stress the following aspects of contraception for the iPledge Program during counseling:

• Why it is important to use 2 methods of birth control, 1 primary and 1 secondary at all times. Younger teens may need more emphasis on this point to fully understand it and comply.
• Emergency contraception. Younger teens may need more explanation from you about the need to take immediate action if they have unprotected sex or if their contraception method fails.

Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Contraception Requirements

Using 2 Methods of Contraception Provides More Protection

Use of 2 iPLEDGE Program approved methods of contraception (at least 1 of which is a primary method) simultaneously substantially reduces the risk that a female will become pregnant.

In addition, it is not known if hormonal contraceptives are less effective when used with isotretinoin.3 Because of this possibility and the fact that all contraceptive methods are less than 100% effective, the iPLEDGE Program requires the additional protection of a second method of contraception.

Selecting an Effective Primary Method of Contraception

Table 1 lists, by typical use failure rate, the primary methods of contraception acceptable in the iPLEDGE Program. The single most important decision in contraception for the iPLEDGE Program is selecting a primary method that the patient can and will use as correctly as possible. Other important factors to consider in counseling the patient on selecting a primary method include side effects, contraindications, and the patient’s ability to use it correctly. All of these factors influence compliance with the iPLEDGE Program requirements to prevent pregnancy.

Hormonal Combination Oral Contraceptives as a Primary Method

If the patient is currently taking or planning to take oral contraceptives, review that section in the Birth Control Workbook with her. For a patient who has indicated she has difficulty taking oral contraceptives correctly, other contraception not requiring daily dosing may be a better choice. It is critical that such a patient choose a method other than daily oral contraceptive agents.
Selecting an Effective Secondary Method of Contraception

Table 2 lists the acceptable secondary methods of contraception in the iPLEDGE® Program. There are 2 methods of secondary contraception: barrier and other. Barrier methods include the diaphragm and cervical cap (both of which must be used with a spermicide) and the male latex condom (which can be used with or without a spermicide). The other method is the vaginal sponge, which contains a spermicide. The most important issue for a secondary method is that it be used correctly each time the patient has intercourse and that it be in place should the primary method fail.

Help the patient select a secondary method that she and her partner can fully commit to using correctly each time they have intercourse.

Reference ID: 4252185
Unacceptable Methods of Contraception

The following methods of contraception are not acceptable for the iPLEDGE Program:
- Progesterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method or fertility awareness)
- Breastfeeding
- Withdrawal
- Cervical shield, a silicone disc with a one-way air valve that creates suction to adhere to the cervix*

Patients currently using these unacceptable methods of contraception must switch to iPLEDGE Program approved methods of contraception.

Emergency Contraception

Review this section in the Birth Control Workbook with the patient. She should know when to call her prescriber for possible emergency contraception. She should also realize that emergency contraception should not be used on a regular basis as a replacement for the other contraceptive methods she selected.

Abstinence

For this program, all females of reproductive potential must fully commit to pregnancy prevention.

Isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE Program. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence, she must understand that she has committed to not engaging in sex or sexual contact with any male 24 hours a day, 7 days a week for 1 month before, during, and for 1 month after she stops taking isotretinoin.

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.

*A cervical shield should not be confused with a cervical cap, which is an effective secondary method of contraception.
About The Referral Form

The Isotretinoin Contraception Referral form, brought in to you by this patient, has been filled out in part by the prescriber. Please fill out the rest of the form at the conclusion of your counseling session and fax or mail the copy back to the prescriber, keeping a copy for your own records.

Reimbursement Form

Also in the back pocket is a reimbursement form for contraceptive counseling services. The iPLEDGE® Program provides reimbursement for 1 contraception counseling session for patients who have been prescribed isotretinoin. Please complete the form and fax it to 1-866-495-0660.

Reporting a Pregnancy

If you become aware of a pregnancy in a patient taking isotretinoin, please report the pregnancy to the iPLEDGE Program by calling 1-866-495-0654 and choosing the option to “Report a Pregnancy.”

Please remind any patient who is pregnant to contact the doctor/prescriber who prescribed her isotretinoin.

REFERENCES


Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
ISOTRETINOIN CONTRACEPTION REFERRAL FORM
Prescriber: Complete for Patients Being Referred for Contraception Counseling

Patient ___________________________________________, iPLEDGE Program ID# _____________.

is considering treatment with isotretinoin. I am referring her for counseling to help her choose her 2 methods
of contraception before she receives her first prescription.

Please complete the Record of Contraception Counseling below and return this form to my office, via fax or mail.
She had a negative (serum/urine) pregnancy test on ________________________

Please review this Contraception Counseling Guide for details on the iPLEDGE Program contraception requirements.

Isotretinoin Prescriber's Name ____________________________________________

Address ________________________________________________________________

Telephone ______-____-____ Fax ______-____-____

Isotretinoin Prescriber's Signature _______________________________________

Date ______________________

RECORD OF CONTRACEPTION COUNSELING
Contraception Counselor: Complete Form and Fax or Mail Back to Isotretinoin Prescriber

I have provided the following for your patient ______________________________________

☐ Comprehensive contraception counseling
☐ Information about emergency contraception

The patient has:

☐ Chosen 2 methods of contraception
☐ Committed to abstain from any sexual contact with a male and is not planning to use 2 methods of
contraception. I informed her that abstinence without using contraception is not recommended
for the iPLEDGE Program for sexually active women.
☐ Not yet decided upon the methods of contraception she will use

Primary Method _________________________________________________________

Secondary or Second Primary Method _______________________________________

I have prescribed the selected contraception.

☐ Yes ☐ No (Please comment below)

I believe that this patient is fully committed to complying with the contraceptive requirements of the
iPLEDGE Program.

☐ Yes ☐ No (Please comment below)

__________________________________________

Name __________________________________________

Address _________________________________________

Telephone _________________________________

Specialty (circle one): OB-GYN  Fam Prac  IM  RN  LPN  Other ______________________

Contraception Counselor’s Signature ______________________________

Date ________________________

Prescriber Copy-White   Contraception Counselor Copy-Yellow   Patient Copy-Pink

Please see accompanying complete product information, including boxed
CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS,
WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

www.ipledgeprogram.com 1-866-495-0654
FAUXABLE REIMBURSEMENT FORM
The Following Restrictions Apply:

Only consulting clinicians who provide initial pregnancy prevention counseling are eligible for reimbursement for such counseling. Other services provided during this visit are not eligible for reimbursement. The physician prescribing isotretinoin, or any other person working under the direct supervision of said physician, is not eligible for this reimbursement provision. The reimbursement fee is up to $150.00, which has been determined to be an average, usual, and customary reimbursement for service of this type. Information will be used only for reimbursement; the isotretinoin manufacturers will not use it for any other purpose.

Reimbursement For Pregnancy Prevention Counseling
To receive reimbursement for providing pregnancy prevention counseling to an isotretinoin patient, please answer the following questions, and sign, date, and send the completed form via fax to: 1-866-495-0660.

Contraception Counselor Name
Payee Name (if different than Contraceptive Counselor)
Office Telephone Number - - - Tax ID Number
Payee Address
City State ZIP

Name of Referring Physician
Office Telephone Number - - -
City State ZIP

Patient’s Name
Patient’s iPLEDGE Program ID Number

☐ I have provided pregnancy prevention counseling to this patient. I have mailed or faxed the record of pregnancy prevention counseling (on reverse side) to the isotretinoin prescriber.

☐ I am not the prescribing physician of isotretinoin to the patient referenced above, nor am I employed by said prescribing physician.

☐ I have not, and will not, bill or submit for reimbursement either directly or indirectly, under Medicaid, Medicare, or similar federal or state healthcare programs, or under any private insurance, HMO, or other healthcare benefit program for the pregnancy prevention counseling services described above.

☐ I attest that all of the above information is accurate and understand that I must check each box above to receive reimbursement.

☐ I have included a signed W-9 Form, or already have a W-9 form on file for payment from iPLEDGE. A blank W-9 form and instructions for completion can be found at www.irs.gov

Signature Date

Reference ID: 4252185
ISOTRETINOIN CONTRACEPTION REFERRAL FORM
Prescriber: Complete for Patients Being Referred for Contraception Counseling

FAXABLE REIMBURSEMENT FORM
The Following Restrictions Apply:
Only consulting clinicians who provide initial pregnancy prevention counseling are eligible for reimbursement for such counseling. Other services provided during this visit are not eligible for reimbursement. The physician prescribing isotretinoin, or any other person working under the direct supervision of said physician, is not eligible for this reimbursement provision. The reimbursement fee is up to $150.00, which has been determined to be an average, usual, and customary reimbursement for service of this type. Information will be used only for reimbursement; the isotretinoin manufacturers will not use it for any other purpose.

Reimbursement For Pregnancy Prevention Counseling
WARNING
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE
Use only isotretinoin products approved by the US Food and Drug Administration.
Obtain your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPledge Program.
Patient Information/Informed Consent (for all patients):
To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.

Read each item below and initial in the space provided if you understand each item and agree to follow your doctor’s instructions. A parent or guardian of a patient under age 18 must also read and understand each item before signing the agreement.

Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I, ____________________________________________________________
   (Patient’s Name)
   understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.
   Initials: ______

2. My doctor has told me about my choices for treating my acne.
   Initials: ______

3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. (Note: There is a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)).
   Initials: ______

4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, “anxious” or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have had other signs of depression while taking isotretinoin.
   Initials: ______

5. Before I start taking isotretinoin, I agree to tell my doctor if I have ever had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.
   Initials: ______

6. Before I start taking isotretinoin, I agree to tell my doctor if, to the best of my knowledge, anyone in my family has ever had symptoms of depression, been psychotic, attempted suicide, or has any other serious mental problems.
   Initials: ______

7. Once I start taking isotretinoin, I agree to stop using isotretinoin and tell my doctor right away if any of the following signs and symptoms of depression or psychosis happen:
   - Start to feel sad or have crying spells
   - Lose interest in activities I once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in my appetite or body weight
   - Have trouble concentrating
   - Withdraw from my friends or family
   - Feel like I have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting myself or taking my own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real
   Initials: ______

8. I agree to return to see my doctor every month I take isotretinoin to get a new prescription for isotretinoin, to check my progress, and to check for signs of side effects.
   Initials: ______

9. Isotretinoin will be prescribed just for me — I will not share isotretinoin with other people because it may cause serious side effects, including birth defects.
   Initials: ______

10. I will not give blood while taking isotretinoin or for 1 month after I stop taking isotretinoin. I understand that if someone who is pregnant gets my donated blood, her baby may be exposed to isotretinoin and may be born with serious birth defects.
    Initials: ______

11. I have read the Patient Introductory Brochure and other materials my provider provided me containing important safety information about isotretinoin. I understand all the information I received.
    Initials: ______

12. My doctor and I have decided I should take isotretinoin. I understand that I must be qualified in the iPLEDGE Program to have my prescription filled each month. I understand that I can stop taking isotretinoin at any time. I agree to tell my doctor if I stop taking isotretinoin.
    Initials: ______

I now allow my doctor _____________________________ to begin my treatment with isotretinoin.

Patient Signature: _____________________________ Date: ____________

Parent/Guardian Signature (if under age 18): _____________________________ Date: ____________

Patient Address _____________________________ Telephone ____________ ____________

Patient Name (print) _____________________________

I have:
• fully explained to the patient, _____________________________ the nature and purpose of isotretinoin treatment, including its benefits and risks
• provided the patient the appropriate educational materials, such as the Patient Introductory Brochure and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin
• answered those questions to the best of my ability

Doctor Signature: _____________________________ Date: ____________

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT’S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.
Patient Information/Informed Consent

About Birth Defects (for female patients who can get pregnant)

To be completed by the patient (and her parent or guardian* if patient is under age 18) and signed by her doctor.

Read each item below and initial in the space provided to show that you understand each item and agree to follow your doctor’s instructions. Do not sign this consent and do not take isotretinoin if there is anything that you do not understand.

* A parent or guardian of a minor patient (under age 18) must also read and initial each item before signing the consent.

________________________
________________________
________________________
(Patient's Name)

1. I understand that there is a very high chance that my unborn baby could have severe birth defects if I am pregnant or become pregnant while taking isotretinoin. This can happen with any amount and even if taken for short periods of time. This is why I must not be pregnant while taking isotretinoin.

Initial: ______

2. I understand that I must not get pregnant one month before, during the entire time of my treatment, and for one month after the end of my treatment with isotretinoin.

Initial: ______

3. I understand that I must avoid sexual intercourse completely, or I must use two separate, effective methods of birth control (contraception) at the same time. The only exceptions are if I have had surgery to remove the uterus (a hysterectomy) or both of my ovaries (bilateral oophorectomy), or my doctor has medically confirmed that I am post-menopausal.

Initial: ______

4. I understand that hormonal birth control products are among the most effective methods of birth control. Combination birth control pills and other hormonal products include skin patches, shots, under-the-skin implants, vaginal rings, and intrauterine devices (IUDs). Any method of birth control can fail. That is why I must use two different birth control methods at the same time, starting one month before, during, and for one month after stopping therapy every time I have sexual intercourse, even if one of the methods I choose is hormonal birth control.

Initial: ______

5. I understand that the following are effective methods of birth control:

<table>
<thead>
<tr>
<th>Primary methods</th>
<th>Secondary methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>• tying my tubes (tubal sterilization)</td>
<td>• male latex condom with or without spermicide</td>
</tr>
<tr>
<td>• male vasectomy</td>
<td>• diaphragm with spermicide</td>
</tr>
<tr>
<td>• intrauterine device</td>
<td>• cervical cap with spermicide</td>
</tr>
<tr>
<td>• hormonal (combination birth control pills, skin patches, shots, under-the-skin implants, vaginal rings)</td>
<td>• vaginal sponge (contains spermicide)</td>
</tr>
</tbody>
</table>

A diaphragm and cervical cap must each be used with spermicide, a special cream that kills sperm.

I understand that at least one of my two methods of birth control must be a primary method.

Initial: ______

6. I will talk with my doctor about any medicines including herbal products I plan to take during my isotretinoin treatment because hormonal birth control methods may not work if I am taking certain medicines or herbal products.

Initial: ______

7. I may receive a free birth control counseling session from a doctor or other family planning expert. My isotretinoin doctor can give me an Isotretinoin Contraception Referral Form for this free consultation.

Initial: ______

My doctor has answered all my questions about isotretinoin and I understand that it is my responsibility not to get pregnant one month before, during isotretinoin treatment, or for one month after I stop taking isotretinoin.

Initial: ______

I now authorize my doctor ____________________________ to begin my treatment with isotretinoin.

Patient Signature: ____________________________ Date: __________

Parent/Guardian Signature (if under age 18): ____________________________ Date: __________

Please print: Patient Name and Address: __________________________________________ Telephone: ____________________________

I have fully explained to the patient, ____________________________, the nature and purpose of the treatment described above and the risks to females of reproductive potential. I have asked the patient if she has any questions regarding her treatment with isotretinoin and have answered those questions to the best of my ability.

Initial: ______

8. I must begin using the birth control methods I have chosen as described above at least one month before I start taking isotretinoin.

Initial: ______

9. I cannot get my first prescription for isotretinoin unless my doctor has told me that I have two negative pregnancy test results. The first pregnancy test should be done when my doctor decides to prescribe isotretinoin. The second pregnancy test must be done in a lab during the first 5 days of my menstrual period right before starting isotretinoin therapy treatment, or as instructed by my doctor. I will then have one pregnancy test in a lab:

• every month during treatment
• at the end of treatment
• and I month after stopping treatment

I must not start taking isotretinoin until I am sure that I am not pregnant, have negative results from two pregnancy tests, and the second test has been done in a lab.

Initial: ______

10. I have read and understand the materials my doctor has provided to me, including the Guide to Isotretinoin for Female Patients Who Can Get Pregnant, Birth Control Workbook and Patient Introductory Brochure.

Initial: ______

11. I must stop taking isotretinoin right away and call my doctor if I get pregnant, miss my expected menstrual period, stop using birth control, or have sexual intercourse without using my two birth control methods at any time.

Initial: ______

12. My doctor provided me information about the purpose and importance of providing information to the iPLEDGE Program should I become pregnant while taking isotretinoin or within one month of the last dose. I understand that if I become pregnant, information about my pregnancy, my health, and my baby’s health may be shared with the makers of isotretinoin, authorized parties who maintain the iPLEDGE Program for the makers of isotretinoin, and government health regulatory authorities.

Initial: ______

13. I understand that being qualified to receive isotretinoin in the iPLEDGE Program means that I:

• have had two negative urine or blood pregnancy tests before receiving the first isotretinoin prescription. The second test must be done in a lab. I must have a negative result from a urine or blood pregnancy test done in a lab repeated each month before I receive another isotretinoin prescription.
• have chosen and agreed to use two methods of effective birth control at the same time. At least one method must be a primary method of birth control, unless I have chosen never to have sexual contact with a male (abstinence), or I have undergone a hysterectomy or bilateral oophorectomy, or I have been medically confirmed to be post-menopausal. I must use two methods of birth control for at least one month before I start isotretinoin therapy, during therapy, and for one month after stopping therapy. I must receive counseling, repeated on a monthly basis, about birth control and behaviors associated with an increased risk of pregnancy.
• have signed a Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) that contains warnings about the chance of possible birth defects if I am pregnant or become pregnant and my unborn baby is exposed to isotretinoin.
• have been informed of and understand the purpose and importance of providing information to the iPLEDGE Program should I become pregnant while taking isotretinoin or within 1 month of the last dose.
• have interacted with the iPLEDGE Program before starting isotretinoin and on a monthly basis to answer questions on the program requirements and to enter my two chosen methods of birth control.

Initial: ______

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT’S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.

www.ipledgeprogram.com | 1-866-495-0654
II.D.2 Patient Understanding

**Patient Comprehension Questions**

<table>
<thead>
<tr>
<th>Program Steps</th>
<th>1. True</th>
<th>2. False</th>
</tr>
</thead>
<tbody>
<tr>
<td>One goal of the iPLEDGE Program is making sure pregnant women do not take isotretinoin</td>
<td>1. True</td>
<td>2. False</td>
</tr>
<tr>
<td>You are in your third month of treatment, in order to get your isotretinoin prescription, you must</td>
<td>1. Have a urine test for infection.</td>
<td>2. Have a negative pregnancy test performed in a laboratory, discuss birth control with your doctor/prescriber and answer questions in the iPLEDGE Program system.</td>
</tr>
<tr>
<td>The confidential iPLEDGE Program Pregnancy Registry collects information on pregnancies that happen during isotretinoin treatment or within 1 month after the last dose</td>
<td>1. True</td>
<td>2. False</td>
</tr>
<tr>
<td>Each month you need to answer questions and:</td>
<td>1. Enter 2 methods of birth control you are using.</td>
<td>2. Do a home pregnancy test to show the pharmacist.</td>
</tr>
<tr>
<td>For 1 month after your last dose, you must use 2 effective methods of birth control together correctly all the time</td>
<td>1. True</td>
<td>2. False</td>
</tr>
<tr>
<td>Your doctor/prescriber tells you that you have to come back 1 month after your final dose. You return to the office to:</td>
<td>1. Get a prescription for 30 days.</td>
<td>2. Talk with your doctor/prescriber about birth control.</td>
</tr>
<tr>
<td>Your doctor/prescriber tells you that you need to have a pregnancy test each month. You would:</td>
<td>1. Refuse the test because you know you are not pregnant.</td>
<td>2. Agree to have a pregnancy test each month because it is important to know if you are pregnant because there is a very high chance of birth defects if an unborn baby's mother takes isotretinoin.</td>
</tr>
<tr>
<td>You must keep your appointment every month because:</td>
<td>1. It is important for you and your doctor/prescriber to interact before you get a maximum 30-day supply of isotretinoin each month.</td>
<td>2. You need to sign a consent form each month.</td>
</tr>
<tr>
<td></td>
<td>2. You need to sign a consent form each month.</td>
<td>3. You need to tell your doctor where to call in your prescription.</td>
</tr>
<tr>
<td>General Contraception Requirements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most women who got pregnant during isotretinoin treatment were using only 1 method of birth control.</td>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol and drugs can make it more difficult to use your birth control properly when having sex.</td>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
<td></td>
</tr>
<tr>
<td>You can change one primary method of birth control for another without talking with your doctor/prescriber first.</td>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
<td></td>
</tr>
<tr>
<td>You can use any 2 methods of birth control for the iPLEDGE Program</td>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
<td></td>
</tr>
<tr>
<td>You are using 2 effective methods of birth control in the month after your last dose. Your partner's male latex condom breaks. You would:</td>
<td>1. Forget about it since you have finished isotretinoin</td>
<td></td>
</tr>
<tr>
<td>2. Call your doctor/prescriber to see if you might need emergency birth control.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Get a home pregnancy test kit to see if you are pregnant.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>While you are taking isotretinoin, you must use 2 effective methods of birth control together correctly all the time</td>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
<td></td>
</tr>
<tr>
<td>You should talk to your doctor/prescriber about birth control:</td>
<td>1. Each month during your office visit.</td>
<td></td>
</tr>
<tr>
<td>2. Only when you have a problem.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Only when you sign the second consent form.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>You have finished your last dose of isotretinoin. Your doctor/prescriber has ordered a pregnancy test. For the next month, you:</td>
<td>1. Continue to use 2 effective methods of birth control together correctly all the time.</td>
<td></td>
</tr>
<tr>
<td>2. Stop using your secondary method because you are not taking isotretinoin.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Go for the pregnancy test at any time during the month.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Birth Defects and Pregnancy**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which of the following are signs you might be pregnant?</td>
<td>1. You miss your menstrual period</td>
</tr>
<tr>
<td></td>
<td>2. You have nausea (generally first thing in the morning), sometimes referred to as morning sickness.</td>
</tr>
<tr>
<td></td>
<td>3. Your breasts feel tender, like at the beginning of a menstrual period.</td>
</tr>
<tr>
<td></td>
<td>4. Any of the above is a sign you might be pregnant.</td>
</tr>
<tr>
<td>The risk for birth defects for a baby whose mother took isotretinoin is</td>
<td>1. So low that you do not have to worry.</td>
</tr>
<tr>
<td></td>
<td>2. Low enough so you do not need birth control.</td>
</tr>
<tr>
<td></td>
<td>3. Very high even if a female patient takes isotretinoin for only a short time.</td>
</tr>
<tr>
<td>You can possibly get pregnant if you have a uterus and ovaries.</td>
<td>1. True</td>
</tr>
<tr>
<td></td>
<td>2. False</td>
</tr>
<tr>
<td>Which of the following birth defects may be caused by isotretinoin?</td>
<td>1. No ears</td>
</tr>
<tr>
<td></td>
<td>2. Heart problems</td>
</tr>
<tr>
<td></td>
<td>3. Small jaw and misshaped head</td>
</tr>
<tr>
<td></td>
<td>4. A child could have any or all of these birth defects.</td>
</tr>
<tr>
<td>You think you may be pregnant and you have taken isotretinoin. You would:</td>
<td>1. Not worry because it was only a few doses.</td>
</tr>
<tr>
<td></td>
<td>2. Stop isotretinoin and call your doctor/prescriber. Even the smallest amount of isotretinoin may cause birth defects.</td>
</tr>
<tr>
<td>It's okay to take isotretinoin when</td>
<td>1. You are using one effective method of birth control.</td>
</tr>
<tr>
<td></td>
<td>2. You are using 2 effective methods of birth control together correctly all the time.</td>
</tr>
<tr>
<td></td>
<td>3. You may be pregnant.</td>
</tr>
<tr>
<td>You cannot get pregnant if:</td>
<td>1. You never have sex with a man.</td>
</tr>
<tr>
<td></td>
<td>2. You miss your hormone shots.</td>
</tr>
<tr>
<td></td>
<td>3. You use only a male latex condom with spermicide.</td>
</tr>
</tbody>
</table>
### Safety Information

<table>
<thead>
<tr>
<th>Statement</th>
<th>Option 1</th>
<th>Option 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>I must not give blood while taking isotretinoin and 1 month after stopping isotretinoin.</td>
<td>1. True</td>
<td>2. False</td>
</tr>
<tr>
<td>I will not share my isotretinoin with anyone.</td>
<td>1. Agree</td>
<td>2. Disagree</td>
</tr>
<tr>
<td>Your neighbor wants to try your isotretinoin. You tell her or him:</td>
<td>1. I must not share isotretinoin.</td>
<td>2. He or she must see a doctor/prescriber who can prescribe isotretinoin.</td>
</tr>
<tr>
<td>The Red Cross calls you to give blood right after your last dose. You tell them:</td>
<td>1. I can never give blood again.</td>
<td>2. I cannot give blood until 1 month after my last dose of isotretinoin.</td>
</tr>
<tr>
<td>The Red Cross calls you to give blood during your first month after your last dose. You tell them:</td>
<td>1. I cannot give blood until 1 month after my last dose of isotretinoin.</td>
<td>2. I can never give blood again.</td>
</tr>
</tbody>
</table>

### Obtaining a Prescription

<table>
<thead>
<tr>
<th>Your pharmacist can fill and dispense your prescription only after:</th>
<th>1. You phone it in.</th>
<th>2. Checking with the iPLEDGE Program system to see if you can get isotretinoin.</th>
<th>3. You email it in.</th>
</tr>
</thead>
<tbody>
<tr>
<td>You can get a prescription for isotretinoin only if:</td>
<td>1. Your pregnancy test is negative.</td>
<td>2. You answered the questions correctly.</td>
<td>3. You entered your 2 methods of birth control and they match the birth control methods entered by your doctor/prescriber.</td>
</tr>
<tr>
<td>You had a pregnancy test on Tuesday for your next prescription. What is the last day you can obtain your prescription?</td>
<td>1. Later that same day (7 hours later)</td>
<td>2. By Friday before the pharmacy closes</td>
<td>3. On Monday of the next week</td>
</tr>
<tr>
<td>You can obtain your prescription any time you want</td>
<td>1. True</td>
<td>2. False</td>
<td></td>
</tr>
<tr>
<td>Your doctor/prescriber has entered your negative pregnancy test result and your two methods of birth control into the iPLEDGE Program system and gives you a prescription. Before you can obtain isotretinoin at a pharmacy you must:</td>
<td>1. Answer your comprehension questions in the iPLEDGE Program system.</td>
<td>2. Schedule your next appointment with your doctor/prescriber</td>
<td>3. Sign your informed consent each month.</td>
</tr>
<tr>
<td>Contraception Choices</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>You missed 2 days taking your birth control pills earlier this week. You would:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. You should call your doctor/prescriber as soon as you realize it.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Have sex whenever you want.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **I have been using birth control pills for 5 years and have not gotten pregnant. Why do I need another method of birth control now?** |
| 1. Any form of birth control can fail |
| 2. The birth defects are too severe to risk getting pregnant |
| 3. Isotretinoin may change how well some methods of birth control work |
| 4. All of these |

| **Birth control pills work best when you take them about the same time every day and do not miss any pills.** |
| 1. True |
| 2. False |

| **You can switch to the progesterone-only mini-pill for your primary method of birth control while you are taking isotretinoin.** |
| 1. True |
| 2. False |

| **Birth control pills may not work as well when you are taking isotretinoin. It is important to:** |
| 1. Take two birth control pills every day. |
| 2. Remember to take your birth control pill about the same time every day and always use a second effective method correctly to help prevent pregnancy. |
| 3. Take your birth control pill only before having sex |

| **I’m using my primary method of birth control exactly as prescribed and my partner uses male latex condoms as the second method. My partner does not have any male latex condoms with him tonight. We would:** |
| 1. Have sex anyway. |
| 2. Wait until he can get a male latex condom. |
| 3. Have sex but use withdrawal. |

| **I’m using my primary method of birth control exactly as prescribed and my partner uses male latex condoms with spermicide as the second method. My partner’s male latex condom breaks. I would:** |
| 1. Not worry about getting pregnant. |
| 2. Worry that I may become pregnant but not do anything. |
| 3. Call my doctor/prescriber to talk about emergency birth control. |

| **My partner has only one male latex condom with him. We would:** |
| 1. Have sex more than once and reuse the male latex condom. |
| 2. Have sex once and wait until he can get more male latex condoms. |
| 3. Have sex but use withdrawal. |

| **For the iPLEDGE Program, male latex condoms can be used with or without a spermicide.** |
| 1. True |
| 2. False |

| **If you use lubricant with a male latex condom, it should be a water-based lubricant.** |
| 1. True |
| 2. False |

<p>| <strong>Your partner should put his male latex condom on:</strong> |
| 1. Any time during sex. |
| 2. As soon as he gets an erection, because waiting too long lets sperm leak out. |
| 3. Only when he remembers. |</p>
<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>You find a rip/tear in your diaphragm after you had sex. You should:</td>
<td>1. Forget about it since you were near your period.</td>
</tr>
<tr>
<td></td>
<td>2. Call your doctor/prescriber to see if you might need emergency birth control.</td>
</tr>
<tr>
<td>For the iPLEDGE Program, diaphragms can be used with or without a spermicide.</td>
<td>1. True</td>
</tr>
<tr>
<td></td>
<td>2. False</td>
</tr>
<tr>
<td>After sex, your diaphragm should stay in place for:</td>
<td>1. 24 hours or more.</td>
</tr>
<tr>
<td></td>
<td>2. 2 to 4 hours</td>
</tr>
<tr>
<td></td>
<td>3. At least 6 hours and up to 24 hours.</td>
</tr>
<tr>
<td>You and your partner want to have sex a second time after you put in your diaphragm. You must:</td>
<td>1. Put spermicide in your vagina again before you have sex.</td>
</tr>
<tr>
<td></td>
<td>2. Have sex again without using more spermicide for up to 24 hours at a time.</td>
</tr>
<tr>
<td></td>
<td>3. Take out your diaphragm and clean it before having sex again.</td>
</tr>
<tr>
<td>Your gynecologist or family doctor needs to check how your diaphragm fits:</td>
<td>1. Every time you have sex.</td>
</tr>
<tr>
<td></td>
<td>2. Every 2 years, or if you gain or lose 10 pounds, or after childbirth or an abortion.</td>
</tr>
<tr>
<td></td>
<td>3. Every 2 months.</td>
</tr>
<tr>
<td>The diaphragm with a spermicide can help prevent:</td>
<td>1. Pregnancy</td>
</tr>
<tr>
<td></td>
<td>2. The spread of HIV/AIDS</td>
</tr>
<tr>
<td></td>
<td>3. The spread of other sexually transmitted infections (STIs)</td>
</tr>
<tr>
<td>I’m using my primary method of birth control exactly as prescribed and a cervical cap with a spermicide as my second method. I forgot my cap at home. I would:</td>
<td>1. Have sex anyway.</td>
</tr>
<tr>
<td></td>
<td>2. Wait until I can use the cervical cap with a spermicide.</td>
</tr>
<tr>
<td></td>
<td>3. Have sex but use withdrawal.</td>
</tr>
<tr>
<td>For the iPLEDGE Program cervical caps can be used with or without a spermicide.</td>
<td>1. True</td>
</tr>
<tr>
<td></td>
<td>2. False</td>
</tr>
<tr>
<td>You cannot use the cervical cap if there is any vaginal bleeding, such as during your menstrual period.</td>
<td>1. True</td>
</tr>
<tr>
<td></td>
<td>2. False</td>
</tr>
<tr>
<td>You and your partner want to have sex a second time after you put in your cervical cap. You do not need to put in more spermicide.</td>
<td>1. True</td>
</tr>
<tr>
<td></td>
<td>2. False</td>
</tr>
<tr>
<td>After sex, your cervical cap should stay in place for:</td>
<td>1. 24 hours</td>
</tr>
<tr>
<td></td>
<td>2. 4 to 8 hours</td>
</tr>
<tr>
<td></td>
<td>3. At least 6 hours and up to 48 hours.</td>
</tr>
<tr>
<td>The cervical cap with spermicide can help prevent:</td>
<td>1. Pregnancy.</td>
</tr>
<tr>
<td></td>
<td>2. The spread of HIV/AIDS</td>
</tr>
<tr>
<td></td>
<td>3. The spread of other sexually transmitted infections (STIs)</td>
</tr>
<tr>
<td>I'm using my primary method of birth control exactly as prescribed and use a vaginal sponge as my second method. I ran out of sponges tonight. My partner and I would:</td>
<td>1. Wait until I can buy more sponges</td>
</tr>
<tr>
<td></td>
<td>2. Have sex anyway.</td>
</tr>
<tr>
<td></td>
<td>3. Have sex but use withdrawal.</td>
</tr>
<tr>
<td>I'm using my primary method of birth control exactly as prescribed, but I forgot to put in my vaginal sponge this one time. I would:</td>
<td>1. Not worry that I could have gotten pregnant.</td>
</tr>
<tr>
<td></td>
<td>2. Worry that I may become pregnant, but do nothing.</td>
</tr>
<tr>
<td></td>
<td>3. Call my doctor/prescriber to talk about emergency birth control.</td>
</tr>
<tr>
<td>The vaginal sponge can help prevent:</td>
<td>1. The spread of HIV/AIDS</td>
</tr>
<tr>
<td></td>
<td>2. The spread of other sexually transmitted infections (STIs)</td>
</tr>
<tr>
<td></td>
<td>3. Pregnancy</td>
</tr>
<tr>
<td>You should insert your sponge:</td>
<td>1. Any time during sex.</td>
</tr>
<tr>
<td></td>
<td>2. Any time up to 30 hours before you have sex.</td>
</tr>
<tr>
<td></td>
<td>3. Only when you remember.</td>
</tr>
<tr>
<td>After sex, your sponge should stay in place for:</td>
<td>1. 24 hours or more.</td>
</tr>
<tr>
<td></td>
<td>2. 2 to 4 hours.</td>
</tr>
<tr>
<td></td>
<td>3. At least 6 hours.</td>
</tr>
<tr>
<td>If you and your partner want to have sex a second time after you put in your sponge:</td>
<td>1. You must put spermicide in your vagina again before you have sex.</td>
</tr>
<tr>
<td></td>
<td>2. You can have sex again without using a new sponge for up to 30 hours at a time.</td>
</tr>
<tr>
<td></td>
<td>3. You must take out your sponge and put in a new one before having sex.</td>
</tr>
<tr>
<td>I have been using the hormonal skin patch perfectly for over a year and have not gotten pregnant. Why do I need another method of birth control now?</td>
<td>1. Any method of birth control can fail.</td>
</tr>
<tr>
<td></td>
<td>2. Using two methods of birth control together all the time drastically reduces the chance that you will get pregnant.</td>
</tr>
<tr>
<td></td>
<td>3. Most female patients who got pregnant during isotretinoin treatment were using only 1 method of birth control.</td>
</tr>
<tr>
<td></td>
<td>4. All of these.</td>
</tr>
<tr>
<td>I have been using the hormonal skin patch, but I was 2 days late changing it. If I have sex my chances of getting pregnant are:</td>
<td>1. Increased</td>
</tr>
<tr>
<td></td>
<td>2. Decreased</td>
</tr>
</tbody>
</table>
I am using the hormonal skin patch exactly as my doctor/prescriber tells me. I should not put it on:

1. My upper outer arm.
2. My stomach or upper body.

The hormonal skin patch works best when you change it every week on the same day each week for 3 weeks.

1. True
2. False

You can get pregnant using the hormonal patch if:

1. It becomes loose or falls off for more than 24 hours.
2. You leave the same hormonal patch on more than one week.
3. Both 1 and 2.

You can get pregnant using the hormonal patch if:

1. True
2. False

My hormonal vaginal ring slipped out and I did not replace it within 3 hours, I:

1. Could get pregnant.
2. Could have sex when I want to, my partner’s male latex condom with spermicide is enough.

I have been using a hormonal vaginal ring for 1 year and have not gotten pregnant. Why do I need another method of birth control now?

1. Any method of birth control can fail.
2. Using two methods of birth control all the time drastically reduces the chance that you will get pregnant.
3. Most female patients who got pregnant during isotretinoin treatment were using only 1 method of birth control.
4. All of these.

I am using the hormonal vaginal ring as my primary method. I can use it with which of the following barrier methods?

1. Cervical cap with spermicide.
2. Male latex condom with or without spermicide.
3. Diaphragm with spermicide.

The hormonal ring works best when you leave it in place for 3 weeks and insert a new ring every 4 weeks on the same day of the week.

1. True
2. False

Pregnancy can happen when you are using a hormonal vaginal ring if:

1. The unopened package containing the hormonal vaginal ring is put into direct sunlight or gets hot.
2. It slips out of your vagina and you do not replace it within 3 hours.
3. It does not stay in your vagina for 3 weeks.
4. You leave it in your vagina for more than 3 weeks.
5. All of these reasons.
<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
</table>
| I have been getting hormone shots for 1 year and have not gotten pregnant. Why do I need another method of birth control now? | 1. Any method of birth control can fail.  
2. Using two methods of birth control all the time drastically reduces the chance that you will get pregnant.  
3. Most female patients who got pregnant during isotretinoin treatment were using only 1 method of birth control.  
4. All of these. |
| You get hormone shots:                                                  | 1. Every 12 weeks  
2. Your dermatologist, gynecologist, family doctor or pharmacist (in some states) can give you a shot.  
3. Both are true. |
| You are using hormonal shots as your primary method of birth control, you should remember: | 1. You are not protected against HIV/AIDS  
2. You need to see your dermatologist, gynecologist, family doctor or pharmacist (in some states) to get the hormonal shot  
3. They might delay your ability to get pregnant after you stop using hormonal shots.  
4. All of the above. |
| One advantage of hormone shots is that they also protect against sexually transmitted infections (STIs). | 1. True  
2. False |
| You have chosen hormone shots as your primary method of birth control. Another acceptable method for you to use would be: | 1. Female condoms  
2. Hormonal IUD  
3. Withdrawal  
4. Male latex condoms |
| You have received a prescription for isotretinoin from your doctor/prescriber but have not had the prescription filled. It is OK to have unprotected sex since you have had a negative pregnancy test. | 1. True  
2. False |
| I have been using an IUD for 3 years and have not gotten pregnant. Why do I need another method of birth control now? | 1. Any method of birth control can fail.  
2. Using two methods of birth control all the time drastically reduces the chance that you will get pregnant.  
3. Most female patients who got pregnant during isotretinoin treatment were using only 1 method of birth control.  
4. All of these. |
| Your IUD needs to be checked by your doctor/prescriber: | 1. Within 3 months after you had it inserted.  
2. If your weight stays the same. |
You have chosen an IUD as your primary method of birth control. Another acceptable method for you to use would be:

- 1. Female condoms
- 2. Hormonal IUD
- 3. Withdrawal
- 4. Male Latex Condoms

I had tubal sterilization (blocking my tubes) 5 years ago and have not gotten pregnant. Why do I need another method of birth control now?

1. Any form of birth control can fail, including tubal sterilization (blocking my tubes).
2. Using two methods of birth control all the time drastically reduces the chance that you will get pregnant.
3. Most female patients who got pregnant during isotretinoin treatment were using only 1 method of birth control.
4. All of these.

My primary method of birth control is tubal sterilization (blocking my tubes). I also need to use a secondary method or another primary method of birth control while I am taking isotretinoin:

1. True
2. False

Important information to know about tubal sterilization (blocking your tubes) is:

1. Tubal sterilization (blocking your tubes) does not protect against sexually transmitted infections (STIs).
2. Tubal sterilization (blocking your tubes) does not require surgery.
3. It is easy to re-open the tubes.

Tubal sterilization (blocking your tubes) is a highly effective method of birth control and does not require use of another effective method of birth control while taking isotretinoin:

1. True
2. False

You have chosen tubal sterilization (blocking your tubes) as your primary method of birth control. Another acceptable method for you to use would be:

1. Female condoms
2. Hormonal IUD
3. Withdrawal
4. None of the above

My only partner had a male vasectomy 5 years ago and I have not gotten pregnant. Why do I need another method of birth control now?

1. Using two methods of birth control all the time drastically reduces the chance that you will get pregnant.
2. Any method of birth control can fail.
3. Most female patients who got pregnant during isotretinoin treatment were using only 1 method of birth control.
4. All of these.

My primary method of birth control is my only partner’s male vasectomy. I also need to use a secondary method or another primary method of birth control while I am taking isotretinoin:

1. True
2. False
### Important Information to Know About Your Partner's Male Vasectomy

<table>
<thead>
<tr>
<th>Important Information to Know About Your Partner's Male Vasectomy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Your partner's male vasectomy does not protect against sexually transmitted infections (STIs).</td>
<td></td>
</tr>
<tr>
<td>2. Your partner's male vasectomy does not require surgery.</td>
<td></td>
</tr>
<tr>
<td>3. It is easy to open the tubes again if your partner wants a child later.</td>
<td></td>
</tr>
</tbody>
</table>

### Your Partner's Male Vasectomy

<table>
<thead>
<tr>
<th>Your Partner's Male Vasectomy is a Highly Effective Method of Birth Control and Does Not Require Use of Another Effective Method of Birth Control While Taking Isotretinoin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
</tr>
</tbody>
</table>

### You Have Chosen Your Partner's Male Vasectomy as Your Primary Method of Birth Control. Another Acceptable Method for You to Use Would Be:

<table>
<thead>
<tr>
<th>You Have Chosen Your Partner's Male Vasectomy as Your Primary Method of Birth Control. Another Acceptable Method for You to Use Would Be</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Female condoms</td>
<td></td>
</tr>
<tr>
<td>2. IUD</td>
<td></td>
</tr>
<tr>
<td>3. Withdrawal</td>
<td></td>
</tr>
<tr>
<td>4. None of the above</td>
<td></td>
</tr>
</tbody>
</table>

### I Have Had Implanted Hormones for 2 Years and Have Not Gotten Pregnant. Why Do I Need Another Method of Birth Control Now?

<table>
<thead>
<tr>
<th>I Have Had Implanted Hormones for 2 Years and Have Not Gotten Pregnant. Why Do I Need Another Method of Birth Control Now?</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Using Two Methods of Birth Control All the Time Drastically Reduces the Chance That You Will Get Pregnant.</td>
<td></td>
</tr>
<tr>
<td>2. Any Method of Birth Control Can Fail.</td>
<td></td>
</tr>
<tr>
<td>3. Most Female Patients Who Got Pregnant During Isotretinoin Treatment Were Using Only 1 Method of Birth Control.</td>
<td></td>
</tr>
<tr>
<td>4. All of These.</td>
<td></td>
</tr>
</tbody>
</table>

### My Primary Method of Birth Control is Implanted Hormones. I Also Need to Use a Secondary Method or Another Primary Method of Birth Control While I Am Taking Isotretinoin.

<table>
<thead>
<tr>
<th>My Primary Method of Birth Control is Implanted Hormones. I Also Need to Use a Secondary Method or Another Primary Method of Birth Control While I Am Taking Isotretinoin.</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
</tr>
</tbody>
</table>

### My Implantable Hormone Will Only Be Effective Through the First Month While I Am Taking Isotretinoin, After That I Only Need to Use One Effective Method of Birth Control for the Rest of My Treatment.

<table>
<thead>
<tr>
<th>My Implantable Hormone Will Only Be Effective Through the First Month While I Am Taking Isotretinoin, After That I Only Need to Use One Effective Method of Birth Control for the Rest of My Treatment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
</tr>
</tbody>
</table>

### You Have Chosen Implantable Hormones as Your Primary Method of Birth Control. Another Acceptable Method for You to Use Would Be:

<table>
<thead>
<tr>
<th>You Have Chosen Implantable Hormones as Your Primary Method of Birth Control. Another Acceptable Method for You to Use Would Be</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Female condoms</td>
<td></td>
</tr>
<tr>
<td>2. Hormonal IUD</td>
<td></td>
</tr>
<tr>
<td>3. Withdrawal</td>
<td></td>
</tr>
<tr>
<td>4. None of the Above</td>
<td></td>
</tr>
</tbody>
</table>

### Abstinence Means That You Commit to Not Having Sex or Sexual Contact with Any Male 24 Hours a Day, 7 Days a Week for 1 Month Before, During, and for 1 Month After Your Isotretinoin Treatment.

<table>
<thead>
<tr>
<th>Abstinence Means That You Commit to Not Having Sex or Sexual Contact with Any Male 24 Hours a Day, 7 Days a Week for 1 Month Before, During, and for 1 Month After Your Isotretinoin Treatment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
</tr>
</tbody>
</table>

### One of the Most Common Causes of Unplanned Pregnancy Is Not Being Able to Avoid Sex (Failing to Maintain Abstinence).

<table>
<thead>
<tr>
<th>One of the Most Common Causes of Unplanned Pregnancy Is Not Being Able to Avoid Sex (Failing to Maintain Abstinence)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. True</td>
<td></td>
</tr>
<tr>
<td>2. False</td>
<td></td>
</tr>
</tbody>
</table>
You planned not to have sex while taking isotretinoin, so you do not use any birth control. If you decide to have sex, you need to:

1. Tell the doctor/prescriber who prescribes your isotretinoin before you engage in sexual activity and make a plan to start your birth control and be sure you are not pregnant.

2. Stop having sex until you use your new birth control method for at least 1 month and have a negative pregnancy test.

3. Start using three methods of effective birth control, just to be sure.

4. 1 and 2 are correct.

You must not take isotretinoin if you cannot follow the birth control requirements of the iPLEDGE Program.

1. True

2. False

Important information to know about birth control pills is:

1. You cannot get pregnant while using birth control pills even if you skip pills.

2. Birth control pills do not protect against sexually transmitted infections (STIs) or HIV/AIDS.

3. There are no side effects from using birth control pills.

The male latex condom can help prevent:

1. Pregnancy.

2. The spread of HIV/AIDS.

3. The spread of other sexually transmitted infections (STIs).

4. All of the above.

For 1 month after your last dose, you must use 2 effective methods of birth control together all the time.

1. True

2. False
Wholesaler Registration Letter

Dear wholesaler or chain drug executive,

The iPLEDGE Program requires annual registration of all wholesalers distributing isotretinoin. For the purposes of the iPLEDGE Program, the term wholesaler refers to a wholesaler and each of its individual distribution centers, a distributor and each of its individual distribution centers, and/or each warehousing chain pharmacy distribution center.

A Registration Form is enclosed with this letter.

Key Elements of the iPLEDGE Program, Which Relate to Your Business Practices:

- The program covers all isotretinoin products (brand and generic)
- To be registered, each wholesaler must agree to meet all iPLEDGE Program requirements for wholesale distribution of isotretinoin products by completing the enclosed agreement
- Wholesalers registered in the iPLEDGE Program will only ship isotretinoin to:
  - Wholesalers registered in the iPLEDGE Program with prior written consent from the manufacturer, or
  - Pharmacies registered with and activated in the iPLEDGE Program
- The registration of wholesalers that do not abide by the terms of the agreement will be revoked after an investigation process, and manufacturers of FDA-approved isotretinoin products will not continue to provide them with isotretinoin for distribution
- Registration in the iPLEDGE Program expires in 12 months and requires re-registration annually.

To Register in the iPLEDGE Program, Mail the Completed Agreement to:

iPLEDGE Program
P.O. Box 29094
Phoenix, AZ 85038

OR

Fax the completed form, using the following iPLEDGE fax number: 1-866-495-0660

We thank you for your support in complying with the iPLEDGE Program.

Sincerely,

iPLEDGE Program Sponsors

Reference ID: 4252185
SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE®. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors, or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lipids, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.
Wholesaler Registration Form On Behalf of the Wholesaler Listed Below, I Acknowledge That:

For the purpose of the iPLEDGE Program, the term wholesaler refers to a wholesaler and each of its individual distribution centers, a distributor and each of its individual distribution centers, and/or each warehousing chain pharmacy distribution center. To distribute isotretinoin, wholesalers must be registered with the iPLEDGE Program and agree to meet all iPLEDGE Program requirements for wholesaler distribution of isotretinoin products. Wholesalers must register with the iPLEDGE Program by signing and returning this agreement that affirms they will comply with all iPLEDGE Program requirements for distribution of isotretinoin. The registration of wholesalers that do not abide by the terms of the agreement will be revoked after an investigation process, and manufacturers of FDA approved isotretinoin products will not continue to provide them with isotretinoin for distribution. Each distribution center operated by a wholesaler must register if they are to distribute isotretinoin. These requirements include:

- Registering prior to distributing isotretinoin and registering annually thereafter
- Distributing only FDA approved isotretinoin product obtained directly from the isotretinoin manufacturers (or delegate) or another registered wholesaler
- Beginning November 1, 2005 only ship isotretinoin to:
  - Wholesalers registered in the iPLEDGE Program with prior written consent from the manufacturer, or
  - Pharmacies licensed in the US and registered and activated in the iPLEDGE Program
- Notifying immediately the isotretinoin manufacturer (or delegate) of any nonregistered and/or nonactivated pharmacy or unregistered wholesaler that attempts to order isotretinoin
- Complying with inspection of wholesaler records by the isotretinoin manufacturer (or delegate) for verification of compliance with the iPLEDGE Program
- Returning to the manufacturer (or delegate) any undistributed product if registration is Permanently Deactivated by the iPLEDGE Program or if the wholesaler chooses to not reregister annually.

An agreement must be completed for each distributor center.

I am authorized to execute this agreement on behalf of the wholesaler (and its distribution centers, if applicable)
Wholesaler Name _______________________________________________________

(Type or Print)

Distribution Center’s DEA# ________________________________________________

Distribution Center’s Address ______________________________________________

Distribution Center’s City __________________________________________________

Distribution Center’s State _______ Distribution Center’s ZIP _________________

Distribution Center’s Phone Number _________________________________________

Distribution Center’s Fax Number __________________________________________

Authorized Representative _________________________________________________

(Print First, MI, Last)

Title _________________________________________________________________

E-mail Address for Key Contact ___________________________________________

E-mail Address for Pharmacy Eligibility File Delivery* _______________________

Authorized Representative’s Signature ______________________________________

Date ______/_____/______

Month Day Year

*The list of registered and activated pharmacies will be e-mailed to this address daily.

This agreement expires 12 months from agreement date. Annual registration is required.
Wholesaler Product Return Letter

Isotretinoin Return Customer Instruction Guide - Wholesaler

Wholesaler Name
Address 1
Address 2
City, State Postal Code

Dear Wholesaler:

You are no longer registered in the iPLEDGE Program for the following reason:

• Your facility is closing, and will no longer be a wholesaler in the iPLEDGE Program.

Therefore, you are required to return all isotretinoin inventories in stock effective immediately.

This action is pursuant to the FDA approval of the iPLEDGE Program through the special restricted distribution program. If you have questions about your status in the iPLEDGE Program, please call 1-866-495-0654 or visit www.ipledgeprogram.com for more information.

**Action required by a wholesaler no longer registered in the iPLEDGE Program:**

• Immediately remove all isotretinoin from your stock.
• If you have isotretinoin inventory, please call 1-866-495-0654 for further instructions on returning this product to the manufacturer.

Sincerely,

iPLEDGE Program Sponsors

www.ipledgeprogram.com | 1-866-495-0654
SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE®. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lipids, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

iPLEDGE, an enhanced pregnancy risk management program designed to minimize fetal exposure to isotretinoin, has been approved by the FDA through a special restricted distribution program.

www.ipledgeprogram.com  1-866-495-0654
REQUESTING PARTY INFORMATION: (Please print or type)
Requester Name: ____________________________________________________ Telephone: _______________
E-Mail Address: _______________________________________________ Date of Request: ________________
Wholesaler Name: _______________________________________________ DEA: _______________________
Address: _____________________________________ City:________________ State:_________ Zip:__________

Requesting Party represents and warrants that the Receiving Party listed below is registered with the iPLEDGE Program.
Requester Signature: ________________________________________ Date: ____________________________

RECEIVING PARTY INFORMATION
Wholesaler Name: ______________________________________________ DEA: ________________________
Address: ______________________________________ City:______________ State:_________ Zip:___________
Ship to Address: _________________________________ City: _________________ State: ______ Zip: ________

MANUFACTURER’S CONSENT
Shipments of [Product Name and Generic Designation] between wholesalers* must be in compliance with
the iPLEDGE Program. Labeling for [Product Name] states that wholesalers registered in the iPLEDGE Program may
only ship to other registered wholesalers with prior written consent from the manufacturer. Pursuant to the labeling for
[Product Name], the authorized signature below shall serve as written consent from the manufacturer provided that
the requesting and receiving party’s registration is verified prior to each shipment. Registration will be verified by
[Manufacturer Name] upon receipt of shipment request.

*The term wholesaler refers to a wholesaler and each of its individual distribution centers, a distributor and each of its
individual distribution centers, and/or each warehousing chain pharmacy distribution center.

NOTE: This Wholesaler to Wholesaler Shipment Request Form is not required when shipping isotretinoin between
distribution centers that are under the same parent company.

[Name of Manufacturer]

By: _____________________________________________________ Title: ______________________________ __

Print Name: ______________________________________________ Date: _________________________________

Please return completed forms to [Insert Appropriate Information Including Fax Number, Email URL, Telephone
Number, etc.]

Please note that this approval is for a one time shipment. Further shipments require consent from
[Manufacturer].
FDA REMS Submission

Patient Screens Inventory

iPLEDGE Program

Revised: December 2017
Patient Screens Inventory:

### Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Registration from Public Home Page</td>
<td>3</td>
</tr>
<tr>
<td>Patient Home Page for Patient in Program Status “Required to Demonstrate Comprehension”</td>
<td>4</td>
</tr>
<tr>
<td>Patient Home Page for Patient Not in Program Status “Required to Demonstrate Comprehension”</td>
<td>5</td>
</tr>
<tr>
<td>Patient – Comprehension Questions- Did not fill Rx in previous window</td>
<td>6</td>
</tr>
<tr>
<td>Patient – Comprehension Questions – Primary (First Time):</td>
<td>10</td>
</tr>
<tr>
<td>Patient – Comprehension Questions – Barrier/Primary (First Time):</td>
<td>11</td>
</tr>
<tr>
<td>Patient – Comprehension Questions – Primary (Subsequent):</td>
<td>12</td>
</tr>
<tr>
<td>Patient – Comprehension Questions – Barrier/Primary (Subsequent):</td>
<td>13</td>
</tr>
<tr>
<td>Comprehension Questions – Sample Question</td>
<td>14</td>
</tr>
<tr>
<td>Patient – Comprehension Question - Correct Answer - SAMPLE:</td>
<td>15</td>
</tr>
<tr>
<td>Patient – Comprehension Question - Incorrect Answer - SAMPLE:</td>
<td>16</td>
</tr>
<tr>
<td>Patient – Comprehension Test Results- SAMPLE: Results: Failed</td>
<td>17</td>
</tr>
<tr>
<td>Patient – Comprehension Test Results- SAMPLE: Results: Passed</td>
<td>18</td>
</tr>
<tr>
<td>Patient – Contraception Information:</td>
<td>19</td>
</tr>
<tr>
<td>Patient – Patient Information</td>
<td>20</td>
</tr>
<tr>
<td>Patient - About Isotretinoin</td>
<td>21</td>
</tr>
<tr>
<td>Patient - About iPLEDGE</td>
<td>22</td>
</tr>
<tr>
<td>Patient – Change Primary Prescriber</td>
<td>23</td>
</tr>
<tr>
<td>Patient – Find a Participating Pharmacy</td>
<td>24</td>
</tr>
<tr>
<td>Patient – Update My Information</td>
<td>25</td>
</tr>
<tr>
<td>Patient – Update My Information – Change Password</td>
<td>26</td>
</tr>
<tr>
<td>Patient – Update My Information – Change DOPS</td>
<td>27</td>
</tr>
<tr>
<td>Patient – Update My Information – Update Contact Information</td>
<td>28</td>
</tr>
<tr>
<td>Patient – My Program Status</td>
<td>29</td>
</tr>
<tr>
<td>Patient – FAQs</td>
<td>30</td>
</tr>
<tr>
<td>Patient – iPLEDGE Terms of Use</td>
<td>31</td>
</tr>
<tr>
<td>Patient – Safety Notice</td>
<td>32</td>
</tr>
</tbody>
</table>
Patient Registration

Patients cannot register directly in the iPLEDGE Program. All Patients are registered in iPLEDGE by a Prescriber. A Prescriber is a medical professional such as a doctor. If you believe you should be registered in the iPLEDGE Program, please contact your Prescriber.
Patient Home Page for Patient in Program Status “Required to Demonstrate Comprehension”

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called PLEDGE®. Under this program, prescribers must be registered and activated with the PLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of PLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with PLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with PLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people have tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin. Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracyclines. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lipids, allergic reactions, blood sugar or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.

Answer the Comprehension Questions Section:

The PLEDGE Program requires you to answer comprehension questions before every prescription. These questions will demonstrate your understanding of the PLEDGE Program requirements, the birth control that you have chosen, and the risks associated with isotretinoin. You may not obtain your prescription until you have correctly answered the questions. You may use your PLEDGE educational kit as a resource as you answer the questions.

How to Report:

Call our toll free number 1-866-495-0654 to report any of the following:

An Adverse Event: If you or someone you know has experienced an adverse event, please call 1-866-495-0654.

A Pregnancy: To report a pregnancy, please call 1-555-495-0654.
Patient Home Page for Patient Not in Program Status “Required to Demonstrate Comprehension”

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE®. Under the program, prescribers must be registered and activated with the PLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of PLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with PLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with PLEDGE.

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Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, kidneys, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.

How to Report

Call our toll free number 1-866-495-0654 to report any of the following:

An Adverse Event: If you or someone you know has experienced an adverse event, please call 1-866-495-0654.

A Pregnancy: To report a pregnancy, please call 1-866-495-0654.
Patient – Comprehension Questions- Did not fill Rx in previous window

Answer Your Questions

Before You Get Started

iPLEDGE Program has no record of you filing a prescription in your prescription window from [month day, year] through [month day, year]. Did you fill your prescription during the prescription window?

- Yes
- No

Note: Your answer will not restrict you from getting your prescription.

Submit

Reminder: Please be sure that your prescriptions are authorized in the iPLEDGE Program system by the Pharmacy. If the Pharmacy does not authorize the prescription in the iPLEDGE Program system, it could result in an unnecessary interruption in your treatment. Ask the Pharmacy if they have authorized this prescription and look for the iPLEDGE Program sticker on your prescription bag. You may find a participating Pharmacy by using the Find a Pharmacy feature on the iPLEDGE Program website.
Answer Your Questions

Please follow these two steps to demonstrate iPLEDGE Program comprehension.

Step 1: Birth Control Verification

Please enter the two methods of birth control that you are using. These must be the same two methods that you have told your Doctor that you are using. The answers you provide are used to determine what questions should be asked in step 2 below.

Additionally, the first month that you answer your questions, you will be asked a series of questions about information and counseling provided to you. There are no wrong answers to these questions. The answers are used to determine how often the iPLEDGE Program materials are shared with patients.

Step 2: Comprehension Questions

In order to get a prescription of isotretinoin, you must demonstrate your understanding of the iPLEDGE Program requirements, the birth control that you have chosen and the risks associated with isotretinoin. You will be shown a series of questions and a list of multiple choice answers for each question. Only one of the answers will be the right answer for each question. If you choose the right answer, you will move on to the next question. If you choose the wrong answer, you will be shown the right answer for that question, and then you will move on to the next question.

When you have answered all the questions, you will be notified right away if you have passed or not. If you did not pass, you will be shown a list of the questions you got wrong and the right answers for those questions. You will also be shown where to find more information on these questions. You may attempt to answer the questions again after reviewing this information.

You will be allowed to obtain your prescription once you have correctly answered these questions.

Continue
If the patient selects abstinence, they will not be allowed to select a second method of birth control.
Patient – Comprehension Questions - Patient Contraception and First Month Questions

Birth Control Verification

All fields listed below are required unless otherwise indicated.
Please select your birth control methods and click the Submit button.

- **Primary**
  - Birth Control Pills

- **Secondary**
  - Male Latex Condom

Did your doctor or anyone in your doctor's office tell you that it is important not to become pregnant while taking isotretinoin?
- ( ) Yes
- ( ) No

Did you receive the isotretinoin Educational Kit for Female Patients Who Can Get Pregnant?
- ( ) Yes
- ( ) No

If yes, did you read
1. The Guide to Isotretinoin for Female Patients Who Can Get Pregnant?
   - ( ) Yes
   - ( ) No

2. The Birth Control Workbook?
   - ( ) Yes
   - ( ) No

Did you watch the video, “Be Prepared, Be Protected” about birth control?
- ( ) Yes
- ( ) No

Did you watch the video, “Be Aware: The Risk of Pregnancy while on Isotretinoin” about the effects of isotretinoin?
- ( ) Yes
- ( ) No

Did your doctor or anyone in your doctor's office offer to refer you to another health care provider for birth control counseling?
- ( ) Yes
- ( ) No

From whom did you receive birth control counseling?
- My doctor
- Another health care provider
- I did not receive birth control counseling

Submit
Birth Control Verification

All fields listed below are required unless otherwise indicated.

Please select your birth control method(s) then click the Submit button.

Primary
- Birth Control Pills
- Hormonal Implant
  - Hormonal IUD
  - Non-hormonal IUD
  - Tubal Sterilization
  - Male Vasectomy
  - Natural Family Planning
  - Hormonal Shot
  - Hormonal Vaginal Ring
  - Hormonal Skin Patch
  - Birth Control Pills (Combination Type)
  - Progestrone-only Mini-pills
  - Abstinence

Do you know that it is important not to become pregnant while taking
an contraceptive method?
- Yes
- No

Did you watch the video, "Be Prepared, Be Protected" about birth control?
- Yes
- No

Did you watch the video, "Be Aware: The Risk of Pregnancy While on Isotretinoin" about the effects of isotretinoin?
- Yes
- No

Did your doctor or anyone in your doctor’s office ever refer you to another health care provider for birth control counseling?
- Yes
- No

From whom did you receive birth control counseling?
- My doctor
- Another health care provider
- I did not receive birth control counseling

Submit
Birth Control Verification

All fields listed below are required unless otherwise indicated.

Please select your birth control methods click the Submit button.

Primary

- Birth Control Pills

Secondary

- Hormonal IUD
- Hormonal IUD
- Non-hormonal IUD
- Tubal Sterilization
- Male Vasectomy
- Natural Family Planning
- Hormonal Shot
- Hormonal Vaginal Ring
- Female Condom
- Hormonal Skin Patch
- Birth Control Pills (Combination Type)
- Progestrone-only Mini-pills
- Male Latex Condom
- Cervical Cap with a Spermicide
- Diaphragm with a Spermicide
- Vaginal Sponge
- Cervical Shield
- Withdrawal

In case you are on Accutane, please answer the following question:

- Yes
- No

Did your doctor or anyone in your doctor’s office offer to refer you to another health care provider for birth control counseling?

- Yes
- No

From whom did you receive birth control counseling?

- My doctor
- Another health care provider
- I did not receive birth control counseling

Submit
Patient – Comprehension Questions – Primary (Subsequent):

Birth Control Verification

All fields listed below are required unless otherwise indicated.

Please select your birth control methods and click the Submit button.

Primary

- Birth Control Pills
- Hormonal Implant
- Hormonal IUD
- Non-hormonal IUD
- Tubal Sterilization
- Male Vasectomy
- Natural Family Planning
- Hormonal Shot
- Hormonal Vaginal Ring
- Hormonal Skin Patch
- Birth Control Pills (Combination Type)
- Progesterone-only Mini-pills
- Abstinence

Submit
Patient – Comprehension Questions – Barrier/Primary (Subsequent):

Birth Control Verification

All fields listed below are required unless otherwise indicated.
Please select your birth control methods click the Submit button.

Primary
Birth Control Pills [ ]

Secondary
Hormonal IUD [ ]
Hormonal Implant
Hormonal IUD
Non-hormonal IUD
Tubal Sterilization
Male Vasectomy
Natural Family Planning
Hormonal Shot
Hormonal Vaginal Ring
Female Condom
Hormonal Skin Patch
Birth Control Pills (Combination Type)
Progestosterone-only Mini-pills
Male Latex Condom
Cervical Cap with a Spermicide
Diaphragm with a Spermicide
Vaginal Sponge
Cervical Shield
Withdrawal

Submit
Comprehension Questions – Sample Question

You are in your third month of treatment, in order to get your isotretinoin prescription, you must:

- Have a urine test for infection.
- Have a negative pregnancy test done in a laboratory, discuss birth control with your doctor and answer questions in the iPLEDGE Program system.

Please select you answer to the question and click Submit.

Please do not use browser's Refresh, Back or Forward buttons when answering the questions, or you may have to start again.
Comprehension Questions

Correct: You have selected the right answer.

Condoms

If you use a lubricant with a male latex condom, it should be a water-based lubricant.

- True
- False
Comprehension Questions

Incorrect Answer: The correct answer is
"Continue to use 2 effective methods of birth control together all the time."

General Contraception Requirements

You have finished your last dose of isotretinoin. Your doctor has ordered a pregnancy test. For the next month, you:

- Continue to use 2 effective methods of birth control together all the time.
- Stop using your secondary method because you are not taking isotretinoin.
- Go for the pregnancy test at any time during the month.

Please do not use browser's Refresh, Back or Forward buttons when answering the questions, or you may have to start again.
Patient – Comprehension Test Results - SAMPLE: Results: Failed

- Results: Failed to Demonstrate Comprehension
- You have answered the following questions incorrectly.

Important Note:
If this is your last month of treatment:
- Remember to continue using the two methods of acceptable birth control for 30 days after the last dosage.
- Get a pregnancy test after the last dosage and 30 days after the last dosage.

Question: One goal of iPLEDGE is making sure pregnant women do not take isotretinoin

Answers:
✔ True
✘ False

Explanation: The correct answer is True. The goal of the iPLEDGE Program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin.

Reference: The Guide to Isotretinoin For Female Patients Who Can Get Pregnant, What is the iPLEDGE Program (see page 4).

Please review the Educational Materials before you answer the questions again.
Comprehension Questions Results

- The questions are complete.
- You may obtain your prescription any time before 11:59 P.M. Eastern Time on m/d/yyyy

Important Note:

If this is your last month of treatment:

- Remember to continue using the two methods of acceptable birth control for 30 days after the last dosage.
- Get a pregnancy test after the last dosage and 30 days after the last dosage.

Click here to return to the home page
Contraception Information

- Safety Information About Isotretinoin
- Birth Control Workbook
- The Guide to Isotretinoin For Female Patients Who Can Get Pregnant
- iPLEDGE Program Birth Control Information Sheet

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Patient Information

About Patient Information

Are you thinking about starting treatment with isotretinoin? You can learn more about isotretinoin and about the iPLEDGE Program by reading the introductory information brochure and the medication guide available below.

View Information Online

You can click on each link to view the material online. Upon clicking on a link, each file will be launched in a new browser window. To view these PDF files, you will need Acrobat Reader.

Patient Information:

- Guide to Isotretinoin for Female Patients Who Can Get Pregnant
- Birth Control Workbooks
- iPLEDGE Program Birth Control Information Sheet
- iPLEDGE Program Check List
- Contraception Counseling Guide and Contraception Referral Form
- Isotretinoin Contraception Referral Form
- Guide to Isotretinoin for Male Patients and Female Patients Who Cannot Get Pregnant
- Safety Information About Isotretinoin
- Dr. Reddy’s Zenatane Medication Guide
- Mylan Amnesteem Medication Guide
- Sun Anebaria Medication Guide
- Teva Claravis Medication Guide
- Akorn Myorisan Medication Guide
- Amneal Isotretinoin Medication Guide

Manufacturer’s Toll-free Numbers

For more information about the specific brands of isotretinoin, call the individual manufacturers at these numbers.

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Company</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amnesteem®</td>
<td>Mylan Pharmaceuticals Inc.</td>
<td>1-800-796-9526</td>
</tr>
<tr>
<td>Claravis®</td>
<td>Teva Pharmaceuticals USA, Inc.</td>
<td>1-800-227-7522</td>
</tr>
<tr>
<td>Myorisan™</td>
<td>Akorn, Inc.</td>
<td>1-800-832-5576</td>
</tr>
<tr>
<td>Absorica™</td>
<td>Sun Pharmaceutical Industries, Inc.</td>
<td>1-800-486-7984</td>
</tr>
<tr>
<td>Zenatane™</td>
<td>Dr. Reddy’s Laboratories, Ltd.</td>
<td>1-888-375-3784</td>
</tr>
<tr>
<td>Amneal isotretinon</td>
<td>Amneal Pharmaceuticals, LLC</td>
<td>1-877-835-5472</td>
</tr>
</tbody>
</table>
CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, microtia, small or absent external auditory canals); eye abnormalities (including microphthalmia, facial dysmorphia, cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicology for further evaluation and counseling.

Special Prescribing Requirements

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE®. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE.
About iPledge

The iPledge Program is a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the FDA. The program strives to ensure that:

- No female patient starts isotretinoin therapy if pregnant
- No female patient on isotretinoin therapy becomes pregnant

This enhanced program is a SINGLE pregnancy risk management program for prescribing and dispensing all isotretinoin products (brand and generic products). The iPledge Program requires registration of all wholesalers distributing isotretinoin, all healthcare professionals prescribing isotretinoin, all pharmacies dispensing isotretinoin, and all male and female patients prescribed isotretinoin. This program is designed to create a verifiable link between the negative pregnancy test and the dispensing of the isotretinoin prescription to the female patient of reproductive potential. The iPledge Program requires that all patients must qualify at the beginning of each month, the prescriber must counsel the patient and document in the iPledge Program system that the patient has been counseled about the risks of isotretinoin.

There are also additional qualification criteria and monthly requirements for female patients of reproductive potential.

As part of the ongoing risk management of isotretinoin products, it is crucial that a female patient of reproductive potential, selects and commits to use two methods of effective contraception simultaneously for one month before, during, and for one month after isotretinoin therapy. She must have 2 negative urine or blood (serum) pregnancy tests with a sensitivity of at least 25 mIU/ml before receiving the initial isotretinoin prescription. The first pregnancy test is a screening test and can be conducted in the prescriber’s office. The second pregnancy test must be done in a CLIA-certified laboratory according to the package insert. Each month of therapy, the patient must have a negative result from a urine or blood (serum) pregnancy test conducted by a CLIA-certified laboratory prior to receiving each prescription.

Each month, the prescriber must enter the female patient’s pregnancy results and the 2 methods of contraception she has been using in the iPledge Program system. The iPledge Program system verifies that all criteria have been met by the prescriber, patient, and pharmacy prior to granting the pharmacy authorization to fill and dispense isotretinoin. The pharmacist must obtain authorization from the iPledge Program system via the internet (www.iPledgeprogram.com), telephone (1-866-495-0654) or through electronic telecommunication verification (via submission of an isotretinoin prescription claim) prior to dispensing each isotretinoin prescription for both male and female patients.
Patient – Change Primary Prescriber

Change Primary Prescriber

If you change your Primary Prescriber, you will not be able to receive prescriptions from your current prescriber. Instead you will be receiving your future prescriptions from your new prescriber.

Please enter any or all search criteria and click the Search button.

First Name
Jane

Last Name
Smith

Phone

City

State
PA

Zip Code

Search

Found

Name
Jane Smith

Address
Blue Bell, PA

Contact
215-254-2246

Showing 1 to 1 of 1 entries

To transfer to this prescriber please click the Commit To Transfer button.

Please note: Your transfer will not be complete until your selected prescriber has accepted you as a patient.

Commit To Transfer

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Patient – Find a Participating Pharmacy

Find a Participating Pharmacy

Please enter any or all search criteria and click the Search button.

<table>
<thead>
<tr>
<th>Zip</th>
<th>City</th>
<th>State</th>
<th>Select</th>
</tr>
</thead>
</table>

Search

Welcome [Unique ID] | Logout
Have Questions? Call our toll-free number 1-866-496-0654

IPLEDGE Privacy Notice and Terms of Use | Safety Notice | Non-Compliance Action Policy | © 2016 IPLEDGE
Patient – Update My Information

Update My Information

- Change Password
- Change Date of Personal Significance
- Update Contact Information
Patient – Update My Information – Change Password

Change Password

All fields below are required unless otherwise indicated.

Old Password

New Password

Confirm New Password

Save Changes

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Patient – Update My Information – Change DOPS

Change Date of Personal Significance

Your Date of Personal Significance is a date that you will be able to remember (such as an anniversary) and will be used to verify your identity if you need to contact the Call Center.

All fields below are required unless otherwise indicated.

Password

Date of Personal Significance: (MM/DD/YYYY)

Confirm Date of Personal Significance: (MM/DD/YYYY)

Save Changes
Patient – Update My Information – Update Contact Information

Update Contact Information

Use this form to edit your contact information. To edit information not displayed on this form, please contact the Call Center.

All fields below are required unless otherwise indicated.

First Name
Girija

Last Name
Doddapaneni

Address
920 Harvest Drive

City
Blue Bell

State
PA
Zip
19422

Phone Number
555-555-5555
Fax (Optional)

Email (Optional)

girija.doddapaneni@ubc.com

Preferred Method of Communication
Select

Cancel
Save Changes
Patient – FAQs

Frequently Asked Questions (FAQ)

iPLEDGE PROGRAM (click topics below for more information)
A. TECHNICAL ASSISTANCE
B. PATIENT
C. ALL USERS
iPLEDGE Privacy Notice and Terms of Use

Version 2.0. Last Revised: 09/17/2015

These Terms of Use apply to all visitors of the prescription drug risk management site located at http://www.ipledgeprogram.com (the "Site"). The iPLEDGE Website is a Registered User-only account portal available through the Site which enables Registered Users to participate with a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the FDA.

This Site is intended for U.S. audiences only. Users who access the Site from outside the U.S. do so at their own initiative and risk and are responsible for compliance with all applicable laws.

"Registered Users" include Patients, Prescribers, Designated Agents, and Pharmacies who have signed up to participate in the iPLEDGE Program. "Patients" are patients that have been prescribed restricted distribution drugs pursuant to the iPLEDGE Program. "Prescribers" are prescribers that prescribe restricted distribution drugs pursuant to the iPLEDGE Program. "Designated Agents" are persons designated by Prescribers to act on their behalf with the iPLEDGE Website. Pharmacies are pharmacies that utilize the iPLEDGE Website to verify a patient's enrollment in iPLEDGE and status before filling a prescription at a retail pharmacy.

These Terms of Use are between a user of any portion of the Site ("you" or "your") and the sponsors of the Site ("iPLEDGE" "we", "us" and "our").

REGISTRATION AND ASSENT

Access to and use of the Site is conditioned upon your assent to these Terms of Use. You are deemed to have assented to these Terms of Use as applicable to the iPLEDGE Website, when you complete the online registration processes required for Registered Users and indicate during the registration process that you accept these Terms of Use along with the Privacy Policy incorporated therein. You are deemed to have accepted these Terms of Use each time you access the Site and each time you use your login credentials to access the iPLEDGE Website portion of the Site. By registering for or otherwise accessing or using the Site, you acknowledge that you have read, understand, and agree to be legally bound by these Terms of Use. These Terms of Use and the Privacy Policy are available during registration for the iPLEDGE Website and on various pages of the Site.

UPDATES

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SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE®. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lipids, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.
FDA REMS Submission

Pharmacy Screens Inventory

iPLEDGE Program

Revised: December 2017
Pharmacy Screens Inventory:

Table of Contents

| Pharmacy – Pharmacy Registration – For Responsible Site Pharmacists (Button) from Public Home Page | 3 |
| Pharmacy Home Page – Suspended Pharmacy log in Page | 4 |
| Pharmacy Home Page - Pharmacy in Program Status “Registered” or activated Pharmacy whose activation expires within 30 days | 5 |
| Pharmacy – Pharmacy Home Page – Activated Pharmacy not within 30 days of expiration | 6 |
| Pharmacy – Activate Pharmacy Registration (1 of 2) | 7 |
| Pharmacy – Activate Pharmacy Registration (2 of 2) | 8 |
| Pharmacy – Pharmacy Information | 9 |
| Pharmacy – About Isotretinoin | 10 |
| Pharmacy – About iPLEDGE | 11 |
| Pharmacy – Fill Prescription – Prescription fill denial | 12 |
| Pharmacy – Fill Prescription – Lookup Patient | 13 |
| Pharmacy – Fill Prescription – Confirm Patient | 14 |
| Pharmacy – Fill Prescription – Request Authorization | 15 |
| Pharmacy – Fill Prescription – Request Authorization | 16 |
| Pharmacy – Fill Prescription – Authorized | 17 |
| Pharmacy – Reverse Prescription | 18 |
| Pharmacy – Reverse Prescription (Forgot the RMA number? link selected) | 19 |
| Pharmacy – Reverse Prescription – Verify RMA | 20 |
| Pharmacy – Reverse Prescription | 21 |
| Pharmacy – Find a Patient | 22 |
| Pharmacy – Find Wholesaler | 23 |
| Pharmacy – My Program Status | 24 |
| Pharmacy – Order Materials | 25 |
| Pharmacy – Update My Information | 26 |
| Pharmacy – Update My Information – Change Password | 27 |
| Pharmacy – Update My Information – Change DOPS | 28 |
| Pharmacy – Find a Participating Pharmacy | 29 |
| Pharmacy – FAQs/How To’s | 30 |
| Pharmacy – iPLEDGE Terms of Use | 31 |
| Pharmacy – Safety notice | 32 |
Pharmacy – Pharmacy Registration – For Responsible Site Pharmacists (Button) from Public Home Page

Pharmacy Registration

Please provide your pharmacy’s NCPDP number and click the Lookup Info button. This will be used as your Username to identify you in the program and for you to login to the iPLEDGE Program system using the phone or internet site.

NCPDP Number:

Enter or confirm your information. All fields listed below are required unless otherwise indicated.

Responsible Site Pharmacist First Name:

Responsible Site Pharmacist Last Name:

Responsible Site Pharmacist License:

Preferred Method of Communication:
- Email
- Phone Number
- Ext (Optional)
- Email (Optional)
- Fax (Optional)

☐ This pharmacy orders isotretinoin directly from one or more of the manufacturers of isotretinoin.

Can your pharmacy management system adjudicate claims?
- Yes

Click the Save and Print button below. This will present a print friendly registration form for your signature. After printing and signing, return the form to the address or fax number found on the form.

Save and Print
Notice!

This pharmacy is currently SUSPENDED from the iPLEDGE Program due to a confirmed act of non-compliance with iPLEDGE Program requirements.

This pharmacy is NOT permitted to participate in the iPLEDGE Program, and is prohibited from ordering isotretinoin and filling isotretinoin prescriptions.

If it is determined that the pharmacy orders any isotretinoin product, dispenses isotretinoin prescriptions or commits any further acts of Non-Compliance with iPLEDGE Program requirements, this pharmacy may be deactivated from the iPLEDGE Program.
Pharmacy Home Page - Pharmacy in Program Status “Registered” or activated Pharmacy whose activation expires within 30 days

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE®. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

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Please refer to the isotretinoin package insert for full prescribing and dispensing instructions.

Activate My Registration

Follow the program steps to activate your pharmacy’s registration.

Remember, you must activate your pharmacy’s registration in the iPLEDGE Program annually. Please click the Activate button below to begin.

Activate

How to Report?

Call our toll free number 1-866-495-0654 to report any of the following:

An Adverse Event: If you or someone you know has experienced an adverse event, please call 1-866-495-0654.

A Pregnancy: To report a pregnancy, please call 1-866-495-0654.

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Reference ID: 4252185
Activated Pharmacy not within 30 days of expiration.

How to Report

Call our toll free number 1-866-495-0654 to report any of the following:

**An Adverse Event:** If you or someone you know has experienced an adverse event, please call 1-866-495-0654.

**A Pregnancy:** To report a pregnancy, please call 1-866-495-0654.
Activate Pharmacy Registration

Activation requires attesting to the following statements in the iPLEDGE Program system:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I will train all pharmacists, who participate in the filling and dispensing of isotretinoin prescriptions, on the iPLEDGE Program requirements.
- I will comply and seek to ensure all pharmacists who participate in the filling and dispensing of isotretinoin prescriptions comply with the iPLEDGE Program requirements described in the booklet entitled Pharmacist Guide, specifically the "Key Information for Pharmacists" section including the following dispensing information:
  - Prescriptions must be obtained no later than the "Do Not Dispense To Patient After" date, and if not obtained, then the RMA must be reversed in the iPLEDGE Program system and the product returned to inventory.
- I understand and will comply with the Non-Compliance Action Policy.
- I will obtain isotretinoin product only from iPLEDGE registered wholesalers.
- I will not sell, buy, borrow, loan or otherwise transfer isotretinoin in any manner to or from another pharmacy.
- I will return to the manufacturer (or delegate) any unused product if the pharmacy is deactivated by the iPLEDGE Program or if the pharmacy chooses to not reactivate annually.
- I will not fill isotretinoin for any party other than a qualified patient.

- I attest to the statements above.
- I do not attest to the statements above.

Submit
Pharmacy Activation Complete

You are now activated in the system. You may now select any of the menu options to the left to begin using the system.

Current Program Status: Activated
Status Expires: MM/DD/YYYY

Finish
Pharmacy Information

About reference materials

The goals of the iPLEDGE Program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin's serious risks and safe-use conditions. The iPLEDGE Program education materials present the program requirements for pharmacists and for patients. There are also patient and program guides available about contraception.

View Information Online

You can click on each link to view the material online. Upon clicking on a link, each file will be launched in a new browser window. To view these PDF files, you will need Acrobat Reader®.

Patient Information:

- **Medication Guides:**
  - Dr. Reddy's Zenatane Medication Guide
  - Mylan Amnesteem Medication Guide
  - Sun Akrasil Medication Guide
  - Teva Carisio Medication Guide
  - Akorn Invisia Medication Guide
  - Amneal isotretinoin Medication Guide

Pharmacy Information:

- Pharmacist Guide
- Patient Introductory Brochure
- Isotretinoin Educational Kit for Female Patients Who Can Get Pregnant
- Isotretinoin Educational Kit for Male Patients and Female Patients Who Cannot Get Pregnant
- Birth Control Workbook
- Pharmacists Action Instruction
- Pharmacy Pocketcard

Lessons Learned:

- About Leftover Medication
- About Birth Control
- About Post-Treatment Pregnancy Testing

Prescriber Information:

- Package Inserts:
  - Dr. Reddy's Zenatane Package Insert
  - Mylan Amnesteem Package Insert
  - Sun Akrasil Package Insert
  - Teva Carisio Package Insert
  - Akorn Invisia Package Insert
  - Amneal Isotretinoin Package Insert

Manufacturers' Toll-free Numbers

For more information about the specific brands of isotretinoin, call the individual manufacturers at these numbers.

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Company</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amnesteem®</td>
<td>Mylan Pharmaceuticals Inc.</td>
<td>1-800-796-9526</td>
</tr>
<tr>
<td>Claravis®</td>
<td>Teva Pharmaceuticals USA, Inc.</td>
<td>1-800-227-7322</td>
</tr>
<tr>
<td>Myoril®</td>
<td>Akorn, Inc.</td>
<td>1-877-254-4331</td>
</tr>
<tr>
<td>Absorica®</td>
<td>Sun Pharmaceutical Industries, Inc.</td>
<td>1-800-406-7084</td>
</tr>
<tr>
<td>Zenatane™</td>
<td>Dr. Reddy's Laboratories, Ltd.</td>
<td>1-888-375-3784</td>
</tr>
<tr>
<td>Amneal isotretin</td>
<td>Amneal Pharmaceuticals, LLC</td>
<td>1-877-835-5472</td>
</tr>
</tbody>
</table>
Pharmacy – About Isotretinoin

About Isotretinoin

CONTRAINDICATIONS AND WARNINGS
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebellar abnormalities, cerebrum malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency, in some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements
Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPledge®, isotretinoin must only be prescribed by prescribers who are registered and activated with the iPledge Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with the iPledge Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPledge Program.
About iPLEDGE

The iPLEDGE Program is a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the FDA. The program strives to ensure that:

- No female patient starts isotretinoin therapy if pregnant.
- No female patient on isotretinoin therapy becomes pregnant.

This enhanced program is a SINGLE pregnancy risk management program for prescribing and dispensing all isotretinoin products (brand and generic products). The iPLEDGE Program requires registration of all wholesalers distributing isotretinoin, all healthcare professionals prescribing isotretinoin, all pharmacies dispensing isotretinoin, and all male and female patients prescribed isotretinoin. This program is designed to create a verifiable link between the negative pregnancy test and the dispensing of the isotretinoin prescription to the female patient of reproductive potential. The iPLEDGE Program requires that all patients meet qualification criteria and monthly program requirements. Before the patient receives his/her isotretinoin prescription each month, the prescriber must counsel the patient and document in the iPLEDGE Program system that the patient has been counseled about the risks of isotretinoin.

There are also additional qualification criteria and monthly requirements for female patients of reproductive potential.

As part of the ongoing risk management of isotretinoin products, it is crucial that a female of reproductive potential selects and commits to use two methods of effective contraception simultaneously for one month before, during, and for one month after isotretinoin therapy. She must have 2 negative urine or blood (serum) pregnancy tests with a sensitivity of at least 25 mIU/mI before receiving the initial isotretinoin prescription. The first pregnancy test is a screening test and can be conducted in the prescriber’s office. The second pregnancy test must be done in a CLIA-certified laboratory according to the package insert. Each month of therapy, the patient must have a negative result from a urine or blood (serum) pregnancy test conducted by a CLIA-certified laboratory prior to receiving each prescription.

Each month, the prescriber must enter the female patient’s pregnancy results and the 2 methods of contraception she has been using in the iPLEDGE Program system. The iPLEDGE Program system verifies that all criteria have been met by the prescriber, patient, and pharmacy prior to granting the pharmacy authorization to fill and dispense isotretinoin. The pharmacist must obtain authorization from the iPLEDGE Program system via the internet (www.ipledgeresource.com), telephone (1-866-495-0654) or through electronic telecommunication verification (via submission of an isotretinoin prescription claim) prior to dispensing each isotretinoin prescription for both male and female patients.
Pharmacy – Fill Prescription – Prescription fill denial

![iPLEDGE](image)

**Notice!**

**DO NOT FILL THIS PRESCRIPTION**

You are **NOT** authorized to fill the prescription. The iPLEDGE Program safety requirements are not currently met. Failure to adhere to this denial may result in this pharmacy being deactivated from the iPLEDGE Program.

You must re-access the iPLEDGE Program System and acquire an RMA for this patient prior to dispensing.

Additional Information:
- Please ask the patient to contact their doctor.

Look Up Patient

All fields below are required unless otherwise indicated.

To obtain authorization to fill and dispense a prescription (including additional strengths for the same patient), enter the required patient information and then click on the **Look Up Patient** button.

**Obtain Prescription Authorization**

- **Patient ID:** 1901201705
- **Data Of Birth (MM/DD/YYYY):** 03/29/1995

**Cancel**  **Clear Info**  **Look up Patient**
Pharmacy – Fill Prescription – Lookup Patient

Fill Prescription

Look Up Patient

All fields below are required unless otherwise indicated.

To obtain authorization to fill and dispense a prescription (including additional strengths for the same patient), enter the required patient information and then click on the Look Up Patient button.

Obtain Prescription Authorization

Patient ID:
1001337906

Date Of Birth (MM/DD/YYYY):
03/29/1989

Cancel  Clear info  Look up Patient
Pharmacy – Fill Prescription – Request Authorization
Pharmacy – Fill Prescription – Authorized

Fill Prescription

Prescription Authorization

Patient ID: 7006031098
Date of Birth: 06/03/1998
Patient Name: iPLEDGE Patient

Pharmacy Instructions
It is recommended that the pharmacist write the date on the sticker and put the sticker on the prescription bag. Please write the RMA number(s) on the prescription or document it in your pharmacy management system for each patient's fill.

AUTHORIZED to be dispensed to the patient until 11:59 PM Eastern Time on 11/10/2016.

If the prescription is not dispensed by this date:

- Reverse the authorization in the iPLEDGE Program system using the Reverse Prescription process
- Return the product to stock

<table>
<thead>
<tr>
<th>RMA</th>
<th>Brand/Strength</th>
<th>Quantity</th>
<th>Days Supply</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>006545705561</td>
<td>Absorica 20 mg capsules 8un</td>
<td>30</td>
<td>30</td>
<td>10931-0116-31</td>
</tr>
<tr>
<td>006545705562</td>
<td>Absorica 40 mg capsules 8un</td>
<td>30</td>
<td>30</td>
<td>10931-0118-31</td>
</tr>
</tbody>
</table>

Showing 1 to 2 of 2 entries 1 10

Note: If more than one strength is required to achieve the desired dosage, an RMA must be obtained for each strength.

Obtain another RMA for additional strength  Finish
Pharmacy – Reverse Prescription – Verify RMA

Verify RMA and Patient Information

Risk Management Authorization (RMA) Number: 610063310703

Associated Product(s):

<table>
<thead>
<tr>
<th>Product</th>
<th>Qty</th>
<th>Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>00378-6661-83</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

Patient ID: 3010161991
Date of Birth: 10/16/1991
Patient Name: Female Patient

Options: Cancel, Back, Continue
Pharmacy – Reverse Prescription

Pharmacy Reverse Prescription

Reverse Prescription Authorization
Risk Management Authorization (RMA) number 2100000310733 has been REVERSED. The product can be returned to stock.
Pharmacy – My Program Status

Pharmacy Program Status

Your Program Status: Activated

Program Status Expiration Date: MM/DD/YYYY
Pharmacy – Update My Information – Change Password
Change Date of Personal Significance

Your Date of Personal Significance is a date that you will be able to remember (such as an anniversary) and will be used to verify your identity if you need to contact the Call Center.

All fields below are required unless otherwise indicated.

Password

Date of Personal Significance: (MM/DD/YYYY)

Confirm Date of Personal Significance: (MM/DD/YYYY)

Save Changes
Pharmacy – Safety notice

SAFETY NOTICE

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Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.
FDA REMS Submission

Designee Screens Inventory

iPLEDGE Program

Revised: December 2017
Designee Screens Inventory:

The following are Designee specific screens and shared Designee and Prescriber screens. Only the initial screen display of the shared Designee and Prescriber screens are included here; complete screen sequences are listed under the Prescriber Screen Inventory document.

Table of Contents

<table>
<thead>
<tr>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Designee Screens Inventory: ..........................................................</td>
</tr>
<tr>
<td>Designee – Designee Home Page: .........................................................</td>
</tr>
<tr>
<td>Designee Activation - Compliance Notice ..............................................</td>
</tr>
<tr>
<td>Designee Activation Complete ...........................................................</td>
</tr>
<tr>
<td>Designee Acting on Behalf of Prescriber - Selected Prescriber Verification</td>
</tr>
<tr>
<td>Designee Acting on Behalf of Prescriber – Register New Patient ...............</td>
</tr>
<tr>
<td>Designee – About Isotretinoin ..............................................................</td>
</tr>
<tr>
<td>Designee – About iPLEDGE .................................................................</td>
</tr>
<tr>
<td>Designee Acting on Behalf of Prescriber – Manage Patients ......................</td>
</tr>
<tr>
<td>Designee – Prescriber Information ........................................................</td>
</tr>
<tr>
<td>Designee – Order Materials ..................................................................</td>
</tr>
<tr>
<td>Designee – Update My Information .........................................................</td>
</tr>
<tr>
<td>Designee – Update My Information – Change Password ............................</td>
</tr>
<tr>
<td>Designee – Update My Information – Change DOPS ....................................</td>
</tr>
<tr>
<td>Designee Acting on Behalf of Prescriber – Update Contact Information - Edit Prescriber Demographics</td>
</tr>
<tr>
<td>Designee Acting on Behalf of Prescriber – Accept Patient ........................</td>
</tr>
<tr>
<td>Designee Acting on Behalf of Prescriber – Manage Delegates/Designees ........</td>
</tr>
<tr>
<td>Designee - My Program Status ................................................................</td>
</tr>
<tr>
<td>Designee – Find a Participating Pharmacy .............................................</td>
</tr>
<tr>
<td>Designee – FAQs ....................................................................................</td>
</tr>
<tr>
<td>Designee – Action Required List ..............................................................</td>
</tr>
<tr>
<td>Designee – iPLEDGE Terms of Use ..........................................................</td>
</tr>
<tr>
<td>Designee – Safety Notice .......................................................................</td>
</tr>
</tbody>
</table>
Select Prescriber

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount even for a short period of time. Potentially, any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE®. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have died as a result. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin cause these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, kidneys, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

Please refer to the isotretinoin package insert for full prescribing and dispensing instructions.

- You must select a Prescriber

Select the radio button next to the Prescriber, then select Continue to work on the Prescriber's behalf.

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>Suffix</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPLEDGE</td>
<td>Prescriber</td>
<td>MD</td>
</tr>
</tbody>
</table>

Showing 1 to 1 of 1 entries

1 10

Cancel Continue
Designee Activation - Compliance Notice

Designee Activation

Compliance Notice

Isotretinoin is teratogenic and must not be used by pregnant women. The goals of the iPLEDGE Program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin's serious risks and safe-use conditions. With these program goals in mind, iPLEDGE data are routinely analyzed to identify actions of Non-Compliance.

Information entered into the iPLEDGE Program system is considered part of the patient's medical record, and can be used to investigate suspected Non-Compliance. Verified Non-Compliance with regard to the iPLEDGE Program requirements can result in Permanent Deactivation from the iPLEDGE Program. Click here to view the Non-Compliance Action Policy.

Prescribers are responsible for all iPLEDGE Program activities performed by their office staff designees. If an office staff designee is found to be non-compliant in the iPLEDGE Program, resulting actions, including possible Permanent Deactivation from the iPLEDGE Program, can include both the designee and the prescriber.

Verified Non-Compliance may be reported to the FDA.

- I acknowledge the statements above.
- I do not acknowledge the statements above.

Submit
Designee Activation Complete

You are now activated in the system.
You may now act on behalf of a prescriber:

Current Program Status: Attested
Status Expires: 08/03/2017

Finish
Designee Acting on Behalf of Prescriber - Selected Prescriber Verification

Selected Prescriber Verification

You are currently acting on behalf of [Prescriber Name].

If you wish to continue select the Manage Patients button below.

You may also select a button from the menu at the left to perform another task.

To select a different prescriber, click on the Select A Different Prescriber button below.
Designee Acting on Behalf of Prescriber – Register New Patient

Register New Patient

Determine Patient Category

Select Patient Category
- Patient is a Female of Reproductive Potential (FRP)
- Patient is a Female NCT of Reproductive Potential (FNRP)
- Patient is a Male

Cancel  Continue
Designee – About Isotretinoin

**About Isotretinoin**

**CONTRAINdications and Warnings**

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 55 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, microtia, small or absent external auditory canals); eye abnormalities (including microphthalmia), facial dysmorphism; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE®. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE.
Designee – About iPLEDGE

About iPLEDGE

The iPLEDGE Program is a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the FDA. The program strives to ensure that:

- No female patient starts isotretinoin therapy if pregnant
- No female patient on isotretinoin therapy becomes pregnant

This enhanced program is a SINGLE pregnancy risk management program for prescribing and dispensing all isotretinoin products (brand and generic products). The iPLEDGE Program requires registration of all wholesalers distributing isotretinoin, all healthcare professionals prescribing isotretinoin, all pharmacies dispensing isotretinoin, and all male and female patients prescribed isotretinoin. This program is designed to create a verifiable link between the negative pregnancy test and the dispensing of the isotretinoin prescription to the female patient of reproductive potential. The iPLEDGE Program requires that all patients meet qualification criteria and monthly program requirements. Before the patient receives his/her isotretinoin prescription each month, the prescriber must counsel the patient and document in the iPLEDGE Program system that the patient has been counseled about the risks of isotretinoin.

There are also additional qualification criteria and monthly requirements for female patients of reproductive potential.

As part of the ongoing risk management of isotretinoin products, it is crucial that a female of reproductive potential selects and commits to use two methods of effective contraception simultaneously for one month before, during, and for one month after isotretinoin therapy. She must have 2 negative urine or blood (serum) pregnancy tests with a sensitivity of at least 25 mIU/mL before receiving the initial isotretinoin prescription. The first pregnancy test is a screening test and can be conducted in the prescriber’s office. The second pregnancy test must be done in a CLIA-certified laboratory according to the package insert. Each month of therapy, the patient must have a negative result from a urine or blood (serum) pregnancy test conducted by a CLIA-certified laboratory prior to receiving each prescription.

Each month, the prescriber must enter the female patient’s pregnancy results and the 2 methods of contraception she has been using in the iPLEDGE Program system. The iPLEDGE Program system verifies that all criteria have been met by the prescriber, patient, and pharmacy prior to granting the pharmacy authorization to fill and dispense isotretinoin. The pharmacist must obtain authorization from the iPLEDGE Program system via the internet (www.ipledrugprogram.com), telephone (1-866-495-0654) or through electronic telecommunication verification (via submission of an isotretinoin prescription claim) prior to dispensing each isotretinoin prescription for both male and female patients.
Designee Acting on Behalf of Prescriber – Manage Patients
**Prescriber Information**

About Prescriber Information:
- The goals of the IPLEDGE Program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacies, and patients about isotretinoin's serious risks and safe use conditions. The resources below present the program requirements and help you prepare and plan treatments with patients during the course of isotretinoin therapy.

View Information Online
- You can click on each link to view the material online. Upon clicking on a link, each file will be launched in a new browser window. To view those PDF files, you will need Adobe Acrobat®.

Prescriber Information:
- Patient Information Manual
- Guide to Best Practices For The IPLEDGE Program
- Prescriber Information Counseling Guide
- Recognizing Panhormone Disorders in Adolescents and Young Adults: A Guide for Prescribers (revised)
- Patient Information/Informed Consent About Birth Defects (for female patients who can become pregnant)
- Patient Information/Informed Consent for all patients
- Prescriber Checklist for Female Patients of Childbearing Potential
- Prescriber Checklist for Male Patients and Female Patients Who Cannot Get Pregnant
- Prescriber Flowchart
- Prescriber Activator Instructions
- Instructions for Reporting and Inquiring Office and Designee

Lessons Learned:
- About Lower Medication
- About Birth Control
- About Post-Treatment Pregnancy Testing

Package Inserts:
- Mylan Amnesteem® Package Insert
- InvisiBead® Package Insert
- Avi-Q® Package Insert
- Surus® Package Insert
- Dr. Reddy’s Zorvasert® Package Insert
- Allergan isotretinoin Package Insert

Patient Information:
- Guide to Isotretinoin for Female Patients Who Can Get Pregnant
- Birth Control Worksheet
- IPLEDGE Program Birth Control Information Sheet/IPLEDGE Program Checklist
- Contraception Counseling Outline and Contraception Referral Form
- Isotretinoin Contraception Material Form
- Guide to Isotretinoin for Male Patients and Female Patients Who Cannot Get Pregnant
- Safety Information About Isotretinoin

Medication Guides:
- Dr. Reddy’s Zorvasert® Medication Guide
- Mylan Amnesteem® Medication Guide
- InvisiBead® Medication Guide
- Avi-Q® Medication Guide
- Surus® Medication Guide
- Allergan isotretinoin Medication Guide

Manufacturers’ Toll-free Numbers

For more information about the specific brands of isotretinoin, call the individual manufacturers at these numbers.

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Company</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amnesteem®</td>
<td>Mylan Pharmaceuticals Inc.</td>
<td>1-800-706-8526</td>
</tr>
<tr>
<td>Claravis™</td>
<td>Teva Pharmaceuticals USA, Inc.</td>
<td>1-800-227-7122</td>
</tr>
<tr>
<td>Mylan®</td>
<td>Avi-Q, Inc.</td>
<td>1-877-254-4381</td>
</tr>
<tr>
<td>Aclaris®</td>
<td>Sun Pharmaceutical Indus.</td>
<td>1-800-606-7664</td>
</tr>
<tr>
<td>Zenatane™</td>
<td>Dr. Reddy's Laboratories Ltd.</td>
<td>1-888-373-3704</td>
</tr>
<tr>
<td>Avi-Q®</td>
<td>Am孤儿 Pharmaceuticals LLC</td>
<td>1-877-635-6472</td>
</tr>
</tbody>
</table>
Designee – Order Materials

Order Materials

Enter quantities you would like to order:

0 IPLEDGE Program Birth Control Information Sheet/PLEDGE Program Checklist (1 to 10 sheets)

0 Prescribing checklist for Female Patients of Reproductive Potential (1 to 3 packs of 50 tear sheets)

0 Prescribing checklist for Male Patients and Female Patients of Non-Reproductive Potential (1 to 3 packs of 50 tear sheets)

0 Educational DVDs: Be Prepared, Be Protected and Be Aware: The Risk of Pregnancy while on Isotretinoin (1 DVD)

0 Patient Introductory Brochure (1 to 3 packages of 5)

0 Isotretinoin Educational Kit for Female Patients Who Can Get Pregnant (1 to 10 kits)

0 Isotretinoin Educational Kit for Male Patients and Female Patients Who Cannot Get Pregnant (1 to 10 kits)

0 Prescriber Isotretinoin Educational Kit (1 Kit)

0 Spanish Patient Introductory Brochure (1 to 3 packages of 5)

0 Spanish Isotretinoin Educational Kit for Female Patients Who Can Get Pregnant (1 to 10 kits)

0 Spanish Isotretinoin Educational Kit for Male Patients and Female Patients Who Cannot Get Pregnant (1 to 10 kits)

Place Order
Designee – Update My Information

Update My Information

- Change Password
- Change Date of Personal Significance
- Edit Prescriber Demographics for: [Please Select Prescriber]
Designee – Update My Information – Change DOPS
Designee Acting on Behalf of Prescriber – Accept Patient

Accept Patient

Please enter the Patient Identification Number of the patient transferring into your care, and click the Look Up button.

Patient Identification Number

Look Up
Designee Acting on Behalf of Prescriber – Manage Delegates/Designees

Manage Delegates and Designees

Delegates
A prescriber can delegate another registered and activated iPLEDGE Program prescriber to cover for him/her during a scheduled absence (travel, vacation, etc.). This also can be used to delegate to another registered and activated prescriber in a multiple doctor practice where a patient may see any of the doctors in the office. Delegate status has an expiration date that can be set by the delegating prescriber.

Designees
A designee is a staff member in the prescriber’s office. A registered designee may perform some patient functions on behalf of the prescriber. An office designee may support some of the registered prescribers in a multi-physician practice and will also have rights for any patient of a delegate prescriber. Each office staff designee will only need to register once, even if they support several prescribers. Also, if a prescriber is not activated in the iPLEDGE Program system, neither the prescriber nor the designated office staff can register a patient. The registered prescriber is responsible for all information entered and activities performed in the iPLEDGE Program by all designees under his/her supervision.
Designee - My Program Status

Designee Program Status

Your Program Status: Attested
Program Status Expiration Date: MM/DD/YYYY
Designee – Find a Participating Pharmacy
Designee – FAQs

Frequently Asked Questions (FAQ)

iPLEDGE PROGRAM (click topics below for more information)
A. TECHNICAL ASSISTANCE
B. PRESCRIBES
C. ALL USERS
Designee – Action Required List

Action Required List

Based on the iPLEDGE Program requirements, listed below are actions that are required. Please provide the required information to ensure completion of all iPLEDGE Program requirements.

<table>
<thead>
<tr>
<th>Name</th>
<th>Message</th>
<th>Take Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown, Cindy</td>
<td>Enter the initial post-therapy Pregnancy Test Results, due upon completion of therapy.</td>
<td>Take Action</td>
</tr>
<tr>
<td>Brown, Sandy</td>
<td>One or both post-therapy Pregnancy Test Results due upon completion of therapy. (at completion and 30 days after completion of therapy) have not been entered into iPLEDGE. The Patient program status will change to Permanently Lost to Follow Up on 01/07/2010 if post-therapy Pregnancy Test Results are not entered.</td>
<td>Take Action</td>
</tr>
<tr>
<td>Dough, Jane</td>
<td>Patient has been in “Registered” status for over 60 days. If no activity occurs, the system will discontinue this patient on 01/03/2010.</td>
<td>Take Action</td>
</tr>
<tr>
<td>Patient, PRP</td>
<td>Post-therapy Pregnancy Test Results are required at completion of therapy and 30 days after completion of therapy. One or both of these post-therapy Pregnancy Test Results are now due.</td>
<td>Take Action</td>
</tr>
<tr>
<td>Patient, Test</td>
<td>During registration, this patient was determined to be a female of reproductive potential (FRP). However, you have requested to register this patient as a female not of reproductive potential (FNR). Please contact the Call Center to discuss reasons for this request and complete this patient’s registration.</td>
<td>Take Action</td>
</tr>
</tbody>
</table>
SAFETY NOTICE

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Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

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Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.
FDA REMS Submission

Prescriber Screens Inventory

iPLEDGE Program

Revised: April 2018
**Prescriber Screens Inventory:**

**Table of Contents**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescriber Registration – For Prescribers (Button) from Public Home Page</td>
<td>7</td>
</tr>
<tr>
<td>Prescriber Registration – Invalid Identifiers DEA Message</td>
<td>8</td>
</tr>
<tr>
<td>Prescriber Home Page – Activated Prescriber not within 30 days of expiration</td>
<td>9</td>
</tr>
<tr>
<td>Prescriber Home Page – Prescriber in Program Status “Registered” or activated Prescriber whose activation expires within 30 days</td>
<td>10</td>
</tr>
<tr>
<td>Prescriber - Prescriber Activation</td>
<td>11</td>
</tr>
<tr>
<td>Prescriber - Prescriber Activation - Compliance Notice</td>
<td>12</td>
</tr>
<tr>
<td>Prescriber - Prescriber Activation Complete</td>
<td>13</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP</td>
<td>14</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP</td>
<td>15</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP</td>
<td>16</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP</td>
<td>17</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP</td>
<td>18</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP – Patient not unique</td>
<td>19</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP</td>
<td>20</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FRP</td>
<td>21</td>
</tr>
<tr>
<td>Prescriber – Register New Patient - FNRP</td>
<td>22</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Acknowledgement</td>
<td>23</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Determine Patient Category Question 1 of 3</td>
<td>24</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Determine Patient Category Question 2 of 3</td>
<td>25</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Determine Patient Category Question 3 of 3</td>
<td>26</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Review Patient Category – System determines patient is FNRP</td>
<td>27</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Patient Information</td>
<td>28</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Patient Information Review</td>
<td>29</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Patient Identification Number</td>
<td>30</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Finish</td>
<td>31</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Continue option to confirm FNRP</td>
<td>32</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Confirm FNRP complete</td>
<td>33</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Review Patient Category – System determines patient is FRP</td>
<td>34</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – FNRP – Request FNRP Status</td>
<td>35</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – MALE</td>
<td>36</td>
</tr>
<tr>
<td>Prescriber - Register New Patient – MALE – Patient Information</td>
<td>38</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FRP – Negative Pregnancy Test</td>
<td>Results</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FRP – Negative PT Results – Finish</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td>Question 1 of 3</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td>Question 2 of 3</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td>Question 3 of 3</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td>Review</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td>Review</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td>Request FNRP</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category</td>
<td>Request FNRP – Finish</td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Discontinue Patient Button – Discontinue Reasons</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Report Pregnancy Button</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Report Pregnancy Button: 1 of 3</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Report Pregnancy Button: 2 of 3</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Report Pregnancy Button: 3 of 3</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Patients – Report Pregnancy Button – Confirmation</td>
<td></td>
</tr>
<tr>
<td>Prescriber – Prescriber Information</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Order Materials</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Update My Information</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Update My Information – Change Password</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Update My Information – Change DOPS</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Update My Information – Contact Info</td>
<td></td>
</tr>
<tr>
<td>Required Information Missing</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Accept Patient</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Delegates/Designees</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Delegates</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Register New Designee</td>
<td></td>
</tr>
<tr>
<td>Prescriber - Manage Designees</td>
<td></td>
</tr>
<tr>
<td>Section</td>
<td>Page</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Prescriber - Program Status</td>
<td>130</td>
</tr>
<tr>
<td>Prescriber - Find a Participating Pharmacy</td>
<td>131</td>
</tr>
<tr>
<td>Prescriber – FAQs</td>
<td>132</td>
</tr>
<tr>
<td>Prescriber – Action Required List</td>
<td>133</td>
</tr>
<tr>
<td>Prescriber – iPLEDGE Terms of Use</td>
<td>134</td>
</tr>
<tr>
<td>Prescriber – Safety Notice</td>
<td>135</td>
</tr>
</tbody>
</table>
Prescriber Registration

Welcome to the iPLEDGE Program.

Have Questions? Call our toll-free number

1-866-369-9604

Prescriber Registration

Attention: This registration page is for licensed prescribers only. If you are a patient, you must be registered in the iPLEDGE Program by your doctor.

Create Prescriber Username

Please provide your DEA number. This will be used as your username to identify you in the program and to log you in to the iPLEDGE Program system using the home or internet site. Your DEA number provided must be your DEA number, not an institutional or student DEA number. Please provide only one DEA number if you have more than one. If you do not have a DEA number, check the box indicating that you would like the program to generate a Username to be used to identify you in the program. This program generated Username will be shipped to you in your prescriber educational kit.

DEA number

or

Generate Username

Prescriber Contact Information

Enter or confirm your information. All fields below are required unless otherwise indicated.

First name

MI (Optional):

Suffix (Optional):

Last name

Specialty (Optional):

Derm.

Practice Name (Optional):

Address

City

State

Zip

Preferred Method of Communication

Email

Phone number

Email (Optional)

Fax (Optional)

Prescriber Identifiers

This notification is to inform you that with the launch of the REMS Pharmacy Network, the iPLEDGE Program will require prescribers to provide a National Provider Identifier (NPI). If your NPI is not on file with the iPLEDGE Program, you will be prompted to enter your NPI upon first log in to the enhanced iPLEDGE Program. Additionally, if you are registered with the Drug Enforcement Administration (DEA), the system will need the entry of your DEA number. Failure to supply these identifiers may result in your patient prescription not being authorized for dispensing.

DEA

NPI

I do not have a DEA

Select Delegates (Optional)

DEA Number or Username

Delegate List

Expiration Date (mm/dd/yyyy)

Add

Remove

Save and Print

Note: this form will print as is. Do not alter text or page layout. All fields must be completed for registration.

Reference ID: 4252185
Prescriber Registration – Invalid Identifiers DEA Message

Information Validation Request

Due to the launch of the enhanced iPLEDGE Program Website, please review and confirm your contact information. This is a one-time request and this message will not appear again once you have confirmed your information.

Continue

Last Name
Smith

Specialty (Optional)
Derm

Practice Name (Optional)

Address
123 Not Drive

City
Blue Bell

State
PA
Zip 18754

Preferred Method of Communication
Email

Phone Number
5555551212

Email (Optional)
test@gmail.com

Fax Number (Optional)

Prescriber Identifiers

This notification is to inform you that with the launch of the REMS Pharmacy Network, the iPLEDGE Program will require prescribers to provide a National Provider Identifier (NPI). If your NPI is not on file with the iPLEDGE Program, you will be prompted to enter your NPI upon first log-in to the enhanced iPLEDGE Program. Additionally, if you are registered with the Drug Enforcement Administration (DEA), the system will require entry of your DEA number. Failure to supply these identifiers may result in your patients’ prescriptions not being authorized for dispensing.

DEA
AB1234567

NPI
1234567890

☐ I do not have a DEA

Cancel   Save Changes

Reference ID: 4252185
SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called iPLEDGE®. Under this program, prescribers must be registered and activated with the iPLEDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of iPLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with iPLEDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with iPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lips, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.

Activate My Registration

Follow the program steps to activate your registration.

Remember, you must activate your registration in the iPLEDGE Program annually. Please click the Activate button below to begin.

How to Report?

Call our toll free number 1-866-485-0654 to report any of the following:

An Adverse Event: If you or someone you know has experienced an adverse event, please call 1-866-485-0654.

A Pregnancy: To report a pregnancy, please call 1-866-485-0654.
Prescriber Activation

Prescribers can only activate their registration by affirming that they meet requirements and will comply with all iPLEDGE Program requirements by attesting to the following points:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I know the risk factors for unplanned pregnancy and the effective measures for avoidance of unplanned pregnancy.
- I have the expertise to provide the patient with detailed pregnancy prevention counseling, or I will refer her to an expert for such counseling, reimbursed by the manufacturer.
- I will comply with the iPLEDGE Program requirements described in the booklet entitled Guide to Best Practices for the iPLEDGE Program and Prescriber Contraception Counseling Guide.
- Before beginning treatment of females of reproductive potential with isotretinoin, and on a monthly basis, the patient will be counseled to avoid pregnancy by using two methods of contraception simultaneously and continuously for at least one month prior to initiation of isotretinoin treatment, during isotretinoin treatment and for one month after discontinuing isotretinoin treatment, unless the patient commits to continuous abstinence.
- I will not prescribe isotretinoin to any female of reproductive potential until verifying she has a negative screening pregnancy test and monthly negative CLIA-certified (Clinical Laboratory Improvement Amendment) pregnancy tests. Patients should have a pregnancy test at the completion of the entire course of isotretinoin and another pregnancy test one month later.
- I will report any pregnancy case that I become aware of while the female patient is on isotretinoin or one month after the last dose to the pregnancy registry.

I attest to the statements above.

I do not attest to the statements above.
Prescriber Activation

Compliance Notice

Isotretinoin is teratogenic and must not be used by pregnant women. The goals of the iPledge Program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin's serious risks and safe-use conditions. With these program goals in mind, iPledge data are routinely analyzed to identify actions of Non-Compliance.

Information entered into the iPledge Program system is considered part of the patient's medical record, and can be used to investigate suspected Non-Compliance. Verified Non-Compliance with regard to the iPledge Program requirements can result in Permanent Deactivation from the iPledge Program. Click here to view the Non-Compliance Action Policy.

Prescribers are responsible for all iPledge Program activities performed by their office staff designees. If an office staff designee is found to be non-compliant in the iPledge Program, resulting actions, including possible Permanent Deactivation from the iPledge Program, can include both the designee and the prescriber.

Verified Non-Compliance may be reported to the FDA.

I acknowledge the statements above.
I do not acknowledge the statements above.

Back Submit
Prescriber - Prescriber Activation Complete

You are now activated in the system. You may now select any of the menu options to the left to begin using the system.

Current Program Status: Attested
Status Expires: MM/DD/YYYY

Finish
### Register New Patient

#### Determine Patient Category

**Select Patient Category**
- [ ] Patient is a Female of Reproductive Potential (FRP)
- [ ] Patient is a Female NOT of Reproductive Potential (FNRP)
- [ ] Patient is a Male

---

**References:**
- [iPLEDGE Privacy Notice and Terms of Use](#)  |  [Safety Notice](#)  |  [Non-Compliance Action Policy](#)  |  © 2016 iPLEDGE
Register New Patient

Enter In-Office Pregnancy Test Results. All fields below are required unless otherwise indicated.

In-Office Pregnancy Test Result:
- In-Office Pregnancy Test is Positive
- In-Office Pregnancy Test is Negative

Date of In-Office Positive or Negative Pregnancy Test (MM/DD/YYYY)

[Cancel] [Continue]
Prescriber - Register New Patient – FRP

Register New Patient

Enter Patient Information:

All fields below are required unless otherwise indicated.

First Name

Last Name

Address

City

State

Zip

Select

Cancel

Continue

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### Register New Patient

**Enter Patient Information for Jane Smith - continued:**

All fields below are required unless otherwise indicated.

<table>
<thead>
<tr>
<th>Category</th>
<th>Review</th>
<th>Pregnancy Result</th>
<th>Patient Info</th>
<th>Uniqueness</th>
<th>Identification</th>
<th>Finish</th>
</tr>
</thead>
</table>

- **Phone Number:**

- **Email (Optional):**

- **Date of Birth (MM/DD/YYYY):**

- **Last Four Digits of Social Security Number:**

  - [ ] Check this box if the patient doesn’t have a social security number.

- **Preferred Method of Communication:**

  - [ ] Select

  - [ ] I have obtained the signed program consent form(s) from the patient.

[ ] Cancel  [ ] Back  [ ] Continue
The patient may not be unique.
Please contact the Call Center at 1-866-495-0654 to obtain an override code.

You may need the patient information below to assist the Call Center Representative in determining patient uniqueness.

Patient Name: Jane Smith
Address: 123 Blue Moon St, Blue Bell, PA 18754-4576
Date of Birth: 4/18/1977
Last Four Digits of Social Security Number: 1977

Please Enter Override Code:

Cancel    Continue
Enter Patient Identification Number for Jane Smith:

All fields below are required unless otherwise indicated.

Please find the patient identification number from the patient education materials, and enter it below.

Patient Identification Number

Patient Identification Number (Type Again)

Cancel  Continue
Register New Patient

Patient Registration is complete for Jane Smith. A password will be mailed to the patient, and should be received within 5 to 10 days.

This patient has a 30-day wait period before she can be confirmed. This 30-day wait period begins on the date of registration. You may confirm this patient on or after mm/dd/yyyy. The patient must be counseled to avoid pregnancy by using two methods of iPLEDGE-approved contraception simultaneously and continuously for at least one month prior to initiation of isotretinoin treatment, unless she commits to continuous abstinence.

Do not give the patient a prescription to fill until after you provide this confirmation.

Finish
Register New Patient

Determine Patient Category:

Select Patient Category:
- Patient is a Female of Reproductive Potential (FRP)
- Patient is a Female NCT of Reproductive Potential (FNRP)
- Patient is a Male

Cancel   Continue
Register New Patient

Determine Patient Category:

You have indicated that this patient is a female. The questions that follow will assign a risk category to this female patient, based on her reproductive potential according to the requirements of the iPLEDGE Program.

All female patients are considered Female of Reproductive Potential (FRP) unless one or more of the following applies:

1. Patient has had a hysterectomy
2. Patient has had a bilateral oophorectomy
3. Patient is post-menopausal

Please note that the following conditions DO NOT qualify a patient to be moved from the FRP risk category:

- Tubal Sterilization
- Male Vasectomy
- Abstinence
- Patient has not had her first period (pre-menarche)
- Patient is currently in menopause (but not yet post-menopause)

Please acknowledge your understanding of the qualification criteria as presented to proceed with assigning a risk category to this patient.

[Cancel] [I Acknowledge]
Prescriber - Register New Patient – FNRP – Determine Patient Category

Question 1 of 3

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>REVIEW</th>
<th>PREGNANCY RESULT</th>
<th>PATIENT INFO</th>
<th>UNIQUENESS</th>
<th>IDENTIFICATION #</th>
<th>FINISH</th>
</tr>
</thead>
</table>

Determine Patient Category:

Has patient had a hysterectomy?

- Yes
- No

Notice!

Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient's classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of Isotretinoin prescribing privileges.

Cancel  Continue
Prescriber - Register New Patient – FNRP – Determine Patient Category
Question 2 of 3

Register New Patient

Determine Patient Category:

Has patient had a bilateral oophorectomy?

- Yes
- No

Notice!
Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient's classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

Cancel  Continue
Register New Patient

Determine Patient Category:

For the iPLEDGE Program, a woman is considered post-menopausal upon cessation of previously occurring menses as a result of ovarian failure with documentation of hormonal deficiency by a certified healthcare provider. (i.e. spontaneous menopause)

Hormonal deficiency should be properly documented in the case of spontaneous menopause as follows:

1. If age > 54 years and with the absence of normal menses: Serum FSH (Follicle Stimulating Hormone) level elevated to within the post-menopausal range based on the laboratory reference range where the hormonal assay is performed.

2. If age < 54 years and with the absence of normal menses: Negative serum or urine-hCG, with concurrently elevated serum FSH (Follicle Stimulating Hormone) level in the post-menopausal range, depressed estradiol (E2) level in the post-menopausal range, and absent serum progesterone level, based on the laboratory reference ranges where the hormonal assays are performed.

Using the definition above, is this patient post-menopausal?

- Yes
- No

Notice!
Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient’s classification. Incorrect classification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

Cancel  Continue
Prescriber - Register New Patient – FNRP – Review Patient Category – System determines patient is FNRP

Review Patient Category:

Based on your responses the iPLEDGE Program system has categorized this patient as follows:
Patient is a Female of NON-Reproductive Potential (FNRP)

Based on the following criteria:

- Is patient a Male? No
- Has patient had a hysterectomy? Yes
- Has patient had a bi-lateral oophorectomy? Yes
- Is this patient post-menopausal? Yes

To confirm the patient category and proceed, click Continue.
To change your responses, click Back.

Notice!
Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient's classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of registration prescribing privileges.
Register New Patient

Enter Patient Information for Jane Smith - continued:

All fields below are required unless otherwise indicated.

- Phone Number
- Ext (Optional)
- Email (Optional)
- Date of Birth (MM/DD/YYYY)
- Last Four Digits of Social Security Number
- Check this box if the patient doesn't have a social security number.
- Preferred Method of Communication
  - Select
  - I have obtained the signed program consent form from the patient.

[Buttons: Cancel, Back, Continue]
Patient Information Review:

Patient Name: Jane Smith
Address: 123 Test Drive, Blue Bell, PA 18754-4578
Phone Number: 555-555-1212
Email: test@aol.com
Preferred Method of Communication: Email
Date of Birth: 4/18/1977
Last Four Digits of Social Security Number: 1977
I have obtained the signed program consent form from the patient.
Enter Patient Identification Number for Jane Smith:

All fields below are required unless otherwise indicated.

Please find the patient identification number from the patient education materials, and enter it below.

Patient Identification Number:

Patient Identification Number (Type Again):
Register New Patient

Patient Registration is complete for Jane Smith.
A password will be mailed to the patient, and should be received within 5 to 10 days.

Before Jane Smith’s can fill a prescription, you must confirm patient counseling in the system. Please click the Continue button below to start the confirmation process.

Otherwise select the Finish button to complete Jane Smith’s registration. Note: you may confirm Jane Smith at a later date using the Manage Patients screen.

Continue

Finish
Confirm Patient Counseling

<table>
<thead>
<tr>
<th>CONFIRM</th>
<th>CONTRACEPTION</th>
<th>PREGNANCY RESULT</th>
<th>FINISH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Identification Number: 3306019966
First Name: Jane
Last Name: Smith
Date of Birth: 06/06/1966

☐ I have counseled this patient on the following:
- Isotretinoin should not be shared with anyone
- Blood should not be donated while taking isotretinoin
- Patient program requirements

☐ Check this box if this is the patient's last month of treatment:

In my opinion, this patient understands and is capable of complying with the requirements of the PLEDGE Program.

☐ Yes
☐ No

Selecting the Continue button confirms that you have provided the monthly counseling to this patient.

Continue Cancel
Confirm Patient Counseling

- Confirm Patient Counseling is Complete.

Identification Number: 3300061900
First Name: Jane
Last Name: Smith
Date of Birth: 06/06/1966

Confirm Patient Counseling is Complete.
The patient's Program Status is Qualified to Receive Drug.
The patient may obtain their prescription at the pharmacy. The patient must obtain the prescription before 11:59 pm Eastern Time on MM/DD/YYYY.

Finish
Prescriber - Register New Patient – FNRP – Review Patient Category – System determines patient is FRP

Register New Patient

Review Patient Category:

Based on your responses the iPLEDGE Program system has categorized this patient as follows:

Patient is a Female of Reproductive Potential (FRP)

Based on the following criteria:

- Is patient a Male? No
- Has patient had a hysterectomy? No
- Has patient had a bi-lateral oophorectomy? No
- Is this patient post-menopausal? No

To confirm the patient category and proceed, click Continue.

To change your responses, click Back.

If your responses are correct, but you still believe this patient to be a Female of NON-Reproductive Potential, click Request FNRP Status.

Back  Continue  Request FNRP Status
Notice!

Your responses indicate that the patient should be registered as a Female of Reproductive Potential (FRP). However you are requesting to register this patient as a Female NOT of Reproductive Potential (FNRP). This must be due to an unusual circumstance or unique medical condition not covered in the definition of FNRP for the iPLEDGE Program.

The following are not reasons to register a patient as an FNRP, and requests based on these reasons will be denied.

- Tubal Sterilization
- Male Vasectomy
- Abstinence
- Patient has not had her first period (pre-menarche)
- Patient is currently in menopause (but not yet post-menopausal)

Please contact the Call Center at 1-866-406-0664 to provide further information. You may be required to provide documentation to support this request.

If this request is denied, the patient will need to be re-registered after a negative pregnancy test. Isotretinoin therapy can only begin 30 days from the date the patient is re-registered.
Prescriber - Register New Patient – MALE
Register New Patient

Enter Patient Information:

First Name [Required]
Last Name [Required]
Address [Optional]
City [Optional]
State [Optional]
Zip [Optional]

Options:
- First Name
- MI (Optional)
- Last Name
- Address
- City
- State
- Zip

Cancel Continue
### Register New Patient

#### Patient Information

**Name:** John Smith  
**Gender:** Male  
**Address:**  
**City:**  
**State:**  
**Zip Code:**  
**Date of Birth:** MM/DD/YYYY

**Phone Number:**  
**Email:** (Optional)

**Last Four Digits of Social Security Number:**

**Preferred Method of Communication:**  
- **Select:**  
- **I have obtained the signed program consent form from the patient:**

---

**Reference ID:** 4252185

---

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Patient Information Review:

- **Patient Name:** John Smith
- **Address:** 123 Test Drive, Blue Bell, PA 18754-4578
- **Phone Number:** 555-555-1212
- **Email:** test@sof.com
- **Preferred Method of Communication:** Email
- **Date of Birth:** 4/18/1977
- **Last Four Digits of Social Security Number:** 1977

I have obtained the signed program consent form from the patient.

Welcome [DEA# or Unique ID]
Logout
Have Questions? Call our toll-free number 1-866-495-9654

Register New Patient

The patient may not be unique.

Please contact the Call Center at 1-866-495-9654 to obtain an override code.

You may need the patient information below to assist the Call Center Representative in determining patient uniqueness.

Patient Name: John Smith
Address: 123 Blue Moon St, Blue Bell, PA 18754-4578
Date of Birth: 4/18/1977
Last Four Digits of Social Security Number: 1977

Please Enter Override Code

Cancel Continue

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Prescriber - Register New Patient – MALE – Identification Number Entry

Register New Patient

Enter Patient Identification Number for John Smith:

All fields below are required unless otherwise indicated.

Please find the patient identification number from the patient education materials, and enter it below.

Patient Identification Number

Patient Identification Number (Type Again)

Cancel  Continue
Register New Patient

Patient Registration is complete for John Smith. A password will be mailed to the patient, and should be received within 5 to 10 days.

Before John Smith can fill a prescription, you must confirm patient counseling in the system. Please click the Continue button below to start the confirmation process.

Notice!

Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient’s classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of Isotretinoin prescribing privileges.

Otherwise select the Finish button to complete John Smith’s registration. Note: You may confirm John Smith at a later date using the Manage Patients screen.

Finish
Prescriber - Register New Patient – MALE – Confirm complete
CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and prematurity births have been reported.

Documented external abnormalities include: skull abnormality, ear abnormalities (including anotia, microtia, or absent external auditory canals), eye abnormalities (including microphthalmia), facial dysmorphia, cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities; cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements

Because of isotretinoin’s teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE®. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE.
About iPLEDGE

The iPLEDGE Program is a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the FDA. The program strives to ensure that:

- No female patient starts isotretinoin therapy if pregnant.
- No female patient on isotretinoin therapy becomes pregnant.

This enhanced program is a SINGLE pregnancy risk management program for prescribing and dispensing all isotretinoin products (brand and generic products). The iPLEDGE Program requires registration of all wholesalers distributing isotretinoin, all healthcare professionals prescribing isotretinoin, all pharmacies dispensing isotretinoin, and all male and female patients prescribed isotretinoin. This program is designed to create a verifiable link between the negative pregnancy test and the dispensing of the isotretinoin prescription to the female patient of reproductive potential.

The iPLEDGE Program requires that all patients meet qualification criteria and monthly program requirements. Before the patient receives his/hers isotretinoin prescription each month, the prescriber must counsel the patient and document in the iPLEDGE Program system that the patient has been counseled about the risks of isotretinoin.

There are also additional qualification criteria and monthly requirements for female patients of reproductive potential.

As part of the ongoing risk management of isotretinoin products, it is crucial that a female of reproductive potential selects and commits to use two methods of effective contraception simultaneously for one month before, during, and for one month after isotretinoin therapy. She must have 2 negative urine or blood (serum) pregnancy tests with a sensitivity of at least 25 mIU/ml before receiving the initial isotretinoin prescription. The first pregnancy test is a screening test and can be conducted in the prescriber’s office. The second pregnancy test must be done in a CLIA-certified laboratory according to the package insert. Each month of therapy, the patient must have a negative result from a urine or blood (serum) pregnancy test conducted by a CLIA-certified laboratory prior to receiving each prescription.

Each month, the prescriber must enter the female patient’s pregnancy results and the 2 methods of contraception she has been using in the iPLEDGE Program system. The iPLEDGE Program system verifies that all criteria have been met by the prescriber, patient, and pharmacy prior to granting the pharmacy authorization to fill and dispense isotretinoin. The pharmacist must obtain authorization from the iPLEDGE Program system via the Internet (www.iPLEDGEprogram.com), telephone (1-866-495-0654) or through electronic telecommunication verification (via submission of an isotretinoin prescription claim) prior to dispensing each isotretinoin prescription for both male and female patients.
Prescriber - Manage Patients

<table>
<thead>
<tr>
<th>Name</th>
<th>ID</th>
<th>DOB</th>
<th>Type</th>
<th>Status</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexandra Viskovitch</td>
<td>1234567890</td>
<td>11/10/1983</td>
<td>FRP</td>
<td>Qualified to Receive Drug</td>
<td>-Select-- Go</td>
</tr>
<tr>
<td>Jane Smith</td>
<td>876543210</td>
<td>11/11/1992</td>
<td>FRP</td>
<td>Required to Demonstrate Comprehension</td>
<td>-Select-- Go</td>
</tr>
<tr>
<td>Janet Smith</td>
<td>3210987654</td>
<td>04/04/1914</td>
<td>FRP</td>
<td>Confirmed Positive</td>
<td>-Select-- Go</td>
</tr>
<tr>
<td>Joe Green</td>
<td>765432100</td>
<td>04/10/1907</td>
<td>Male</td>
<td>Registered</td>
<td>-Select-- Go</td>
</tr>
<tr>
<td>Lisa White</td>
<td>9876543210</td>
<td>04/10/1907</td>
<td>FNRP</td>
<td>Registered</td>
<td>-Select-- Go</td>
</tr>
</tbody>
</table>

Showing 1 to 5 of 5 entries

Confirm Patient Counseling

Check Patient Status
Post-therapy Pregnancy Test
Re-register Patient
Discontinue patient
Edit Patient demographics
Edit Patient contraception
Report Pregnancy
Request Exemption
Change Patient Type
Report Tanner Stage Change
Exemption for Female Patients With Serious Medical Reasons

Exemption Option 1 – Tanner Stage 1 or 2
- By selecting this option I attest that all of the following apply to this patient:
  - Classified as Tanner Stage 1 or 2
  - Not considered to be of reproductive potential
  - Not currently pregnant
  - I will evaluate this patient’s reproductive status while receiving isotretinoin and I will notify the PLEDGE Program within 10 business days of any change in the patient’s reproductive status

Exemption Option 2 – Expedite Start of Treatment
- By selecting this option I attest that all of the following apply to this patient:
  - Medical condition necessitates that she be exempt from the initial wait period
  - Not currently pregnant
  - Required to take monthly pregnancy tests
  - Required to successfully complete monthly comprehension testing
  - I understand that the patient will have 7 days to fill her prescription from the date of the monthly pregnancy test specimen collection

Exemption Option 3 – Cognitively and/or Physically Impaired
- By selecting this option I attest that all of the following apply to this patient:
  - Medical condition necessitates that she be exempt from the initial wait period and the monthly comprehension testing
  - Not currently pregnant
  - Required to take monthly pregnancy tests
  - I understand that the patient will have 7 days to fill her prescription from the date of the monthly pregnancy test specimen collection

Cancel  Continue
Exemption for Female Patients With Serious Medical Reasons

Notice!

The intention of this form is to request an exemption from the iPLEDGE requirements for a non-pregnant patient with serious medical reason(s) who is unable to obtain an isotretinoin prescription by completing the requirements in the iPLEDGE Program at this time. It is NOT intended to replace the requirements of the iPLEDGE Program.

Please make certain that you maintain medical documentation supporting the reason(s) for this exemption. The iPLEDGE Program may require a copy.

The medical exemption process is governed by the iPLEDGE Non-Compliance Action Policy. Intentional misuse of the medical exemption process may result in the Permanent Deactivation from the iPLEDGE Program resulting in a permanent loss of isotretinoin prescribing privilege.

I attest that I am both qualified and have performed the necessary medical evaluation(s) to determine that the medical exemption is appropriate for this patient based on the iPLEDGE requirements.

Electronic Signature

Please type your first and last name exactly as it is shown here <insert of DB name> in the signature box to attach your legally binding electronic signature to this exemption request.

Cancel Confirm
Prescriber - Manage Patients – Report Tanner Stage Change button

Tanner Stage 1 or 2 Classification Change Notification

This patient has now advanced beyond Tanner Stage 2 and all of the following apply to this patient:
- Considered to be of reproductive potential
- Not currently pregnant
- Now required to take monthly pregnancy tests
- Now required to successfully complete monthly comprehension testing
- I understand that the patient will have 7 days to fill her prescription from the date of the monthly pregnancy test specimen collection

Continue  Cancel
Program Status Descriptions by Patient Type

Females of Reproductive Potential

Registered

This is a patient who has been entered (registered) into the system by an activated prescriber. The patient will remain in this status for 1 month while she uses her two chosen methods of effective contraception before she can start the qualification process for a prescription.

or

This patient did not obtain her prescription in her first 7-day prescription window, and must now wait a minimum of 19 days between pregnancy tests (with the second pregnancy test in the first 5 days of her menstrual cycle).

or

This patient was using abstinence to meet the requirements of the iFLEDE Program, but will now be using two other methods of contraception. This patient must be on the new methods of contraception for 30 days before she can get her next prescription.

or

This patient’s risk category was previously changed from female of non-reproductive potential, but is still waiting for entry of an initial pregnancy test.

or

A patient that was determined to be a female of reproductive potential during the registration process, but there is a pending request to assign a risk category of female of non-reproductive potential due to special medical circumstances.

Required Action

After the required number of days (30 days if the patient was newly registered, or at least 19 days between pregnancy tests if she did not obtain a prescription in her first 7-day prescription window), the prescriber must confirm the monthly counseling of the patient and enter pregnancy test results for the patient using the Confirm Patient Counseling feature on the Manage Patient screen or through the automated phone system. Entering the pregnancy test results begins the 7-day prescription window for prescription filling and dispensing, meaning the prescription must be obtained within 7 days of the specimen draw date for the pregnancy test. Upon confirmation of the monthly counseling and entry of the pregnancy test results, the patient’s status will change to “Required to Demonstrate Comprehension”. If the registration is pending review for requested female of non-reproductive potential status, this patient cannot be confirmed until the request is reviewed and accepted through discussion with the iFLEDE Program Call Center.
Prescriber - Manage Patients – Confirm Patient Counseling Button – FRP -
Confirm

Confirm Patient Counseling

- Identification Number: 30606556
- First Name: Jane
- Last Name: Smith
- Date of Birth: 06/06/1966

- I have obtained the signed program consent form(s) from the patient.
- I have counseled this patient on the following:
  - Requirement to use two methods of contraception simultaneously and continuously for at least one month prior to initiation of isotretinoin treatment, during isotretinoin treatment and for one month after discontinuing isotretinoin treatment, unless the patient commits to continuous abstinence.
  - Isotretinoin should not be shared with anyone.
  - Blood should not be donated while taking isotretinoin.
  - Patient program requirements.
- Check this box if this is the patient's last month of treatment.

In my opinion, this patient understands and is capable of complying with the requirements of the iPLEDGE Program.

Select

Yes
No

Selecting the Continue button confirms that you have provided the monthly counseling to this patient.

Cancel
Continue
Confirm Patient Counseling

Identification Number: 3703091067
First Name: Jane
Last Name: Smith
Date of Birth: 03/09/1967

Please enter the forms of contraception:

Primary: 

Secondary: 

Select:

I have provided Contraception Counseling to this patient
This patient was referred to and obtained Contraception Counseling from another Health Care Provider

Cancel  Back  Continue
A secondary method will not be allowed to be entered if abstinence is selected as the primary method.
Confirm Patient Counseling

Identification Number: 3703091967
First Name: Jane
Last Name: Smith
Date of Birth: 03/09/1967

Important Information

Note - The confirmatory pregnancy test (just prior to the patient starting isotretinoin therapy) should be performed during the first 5 days of the patient's menstrual cycle.

Continue
Prescriber - Manage Patients – Confirm Patient Counseling Button – FRP – Pregnancy Result (after closing of popup message)
Confirm Patient Counseling

Identification Number: 3304181997
First Name: Jane
Last Name: Smith
Date of Birth: 04/10/1997

Pregnancy Test Specimen collected on: [ ]

Pregnancy Test Type: [ ]
Qualitative Serum
[ ]
Quantitative Serum

Lab Test Results: [ ]
Qualitative Serum
[ ]
Unine

Prescriber Diagnosis: [ ]

Cancel  Back  Continue
Prescriber - Manage Patients – Confirm Patient Counseling Button – FRP – Pregnancy Result (after confirming receipt of laboratory test): 2 of 3

Confirm Patient Counseling

Identification Number: 3304181997
First Name: Jane
Last Name: Smith
Date of Birth: 04/18/1997

Pregnancy Test Specimen collected on:

Pregnancy Test Type:

Lab Test Results:
Select: Positive
Select: Negative

Prescriber Diagnosis:
Select:

Cancel  Back  Continue
Confirm Patient Counseling

- Confirm Patient Counseling is Complete.

Identification Number: 3304181997
First Name: Jane
Last Name: Smith
Date of Birth: 04/18/1997

Confirm Patient Counseling is Complete.
The patient's Program Status is Required to Demonstrate Comprehension.
The patient must answer her Comprehension questions, and then may have her prescription filled before 11:59 PM Eastern Time on 6/7/2015.

Finish
Confirm Patient Counseling

Identification Number: 3364041914
First Name: John
Last Name: Smith
Date of Birth: 04/04/1914

☐ I have counseled this patient on the following:
  - Isotretinoin should not be shared with anyone
  - Blood should not be donated while taking isotretinoin
  - Patient program requirements

☐ Check this box if this is the patient's last month of treatment.

In my opinion, this patient understands and is capable of complying with the requirements of the iPLEDGE Program.

☐ Yes
☐ No

Selecting the "Continue" button confirms that you have provided the monthly counseling to this patient.

Cancel  Continue
Confirm Patient Counseling

- Confirm Patient Counseling is Complete.

Identification Number: 3307019777
First Name: John
Last Name: Smith
Date of Birth: 07/07/1977

Confirm Patient Counseling is Complete.
The patient's Program Status is Qualified to Receive Drug.
The patient may obtain their prescription at the pharmacy. The patient must obtain the prescription before 11:59 PM Eastern Time on MM/DD/YYYY.

Finish
Prescriber - Manage Patients – Edit Patient Contraception Button. Patient is in Window 1, or previous prescription window contraception selection is non-Abstinence.

### Change Contraception Choices

<table>
<thead>
<tr>
<th>Identification Number:</th>
<th>3793091967</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name:</td>
<td>Jane</td>
</tr>
<tr>
<td>Last Name:</td>
<td>Smith</td>
</tr>
<tr>
<td>Date of Birth:</td>
<td>03/09/1967</td>
</tr>
<tr>
<td>Current Program Status:</td>
<td>Required to Demonstrate Comprehension</td>
</tr>
</tbody>
</table>

**Current contraception methods:**

- **Primary:** Birth Control Pills
- **Secondary:** Male Latex Condom

**Please enter patient's new contraception methods. All fields below are required unless otherwise indicated.**

- **Primary:** Birth Control Pills
- **Secondary:** Male Vasectomy

[Cancel] [Save Changes]
Prescriber - Manage Patients – Edit Patient Contraception Button. Patient’s previous prescription window contraception selection is Abstinence.
Enter Post-therapy Pregnancy Test Results

Identification Number: 30111101981
First Name: Jenna
Last Name: Jones
Date of Birth: 11/10/1991
Current Program Status: Permanently Lost to Follow Up

Enter the Specimen Collection Date:

[ ] Jun / [ ] / [ ]

[ ] Continue [ ] Cancel
Prescriber - Manage Patients – Post-therapy Pregnancy Test Button – Pregnancy Test Type

Enter Post-therapy Pregnancy Test Results

Identification Number: 30111101991
First Name: Jane
Last Name: Smith
Date of Birth: 11/18/1991
Current Program Status: Post Therapy

Confirm the Specimen Collection Date:
Specimen Collection Date you entered is: 6/1/2015

These results will be entered as an Initial Post Therapy Pregnancy Test. The 30 day post therapy pregnancy test must have a specimen collection date on or after 7/1/2015.

- Confirm the Specimen Collection Date

Enter the Pregnancy Test Results

- Quantitative Serum
  - Serum HCG: 0.2 mIU/mL

- Qualitative Serum

- Urine

Lab Test Results:
- Positive
- Negative

Prescriber Diagnosis:
- Positive
- Not Pregnant

[Buttons: Cancel, Back, Continue]
Enter Post-therapy Pregnancy Test Results

These results have been successfully entered as an Initial Post Therapy Pregnancy Test. The 30 day post therapy pregnancy test is due with a specimen collection data on or after 7/1/2015.

Finish
Patient Program Status as of 6/1/2015 2:44 PM Eastern Time

Name: Jane Smith
Program Status: Required to Demonstrate Comprehension
Action: No prescriber action is required at this time.

Information: Before the patient can fill and pick up her prescription, she must demonstrate her iPLEDGE comprehension by answering questions in the system. This can be done anytime before the 7-day prescription window expires.

June 2015

<table>
<thead>
<tr>
<th>Sun</th>
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Key:
- Today or future day for an active 7 day window
- A past day for a 7 day window
- A 7 day window that has expired without prescription fill
- Action may occur on this date or any date after

You may click on underlined text to perform the required action.
Patient Program Status Screen – More Information

Name: rayTest10g
Program Status: Medically impaired requires confirmation
Action: Confirm Patient

Information: The patient must have a pregnancy test and be counseled by you. You must confirm this counseling and enter the results of the pregnancy test in the iPLEDGE system. This can occur immediately.

More Information

This is the first day that the patient can have a pregnancy test performed before getting an isotretinoin prescription filled.

For a female of reproductive potential, medically impaired patient (MIP), there are two steps required for each prescription of isotretinoin.

The first step is for the patient to obtain a CLIA certified pregnancy test to ensure they are not pregnant.

The second step is counseling by the prescriber. The prescriber must confirm this counseling in the iPLEDGE system.

The results of the pregnancy test will be entered in the system by the prescriber as part of the confirmation.

Confirmation, including entering the results of the pregnancy test and confirming patient counseling in the system by the prescriber creates the 7-day prescription window. The 7-day prescription window is the duration of time that the patient is allowed to obtain the prescription if they have successfully completed the two steps.

Once the prescriber has confirmed counseling in the system, the patient will be Qualified to Receive Drug. This means the patient may obtain their prescription at the pharmacy before 11:59 PM Eastern Time on the last day of the 7-day prescription window. The pharmacy is not allowed to fill or dispense the prescription after the window ends. The date of the pregnancy test as entered in the system by the prescriber becomes Day 1 of the 7-day prescription window.

The patient will need to start the two steps over, including another CLIA certified pregnancy test, if the prescription is not obtained during the 7-day prescription window.

The expiration date of the current 7-day prescription window can be found on the Patients Program Status page.

Once the prescriber has entered the pregnancy test results and has confirmed counseling in the iPLEDGE system, this calendar will show the 7-day prescription window.
Patient Program Status as of 6/1/2015 3:46 PM Eastern Time

Name: Jenna Jones
Program Status: Registered
Action: No prescriber action is required at this time.

Information: This patient's 7-day prescription window expired, and it was her first window of therapy. Since her first prescription must be preceded by two negative pregnancy tests at least 19 days apart, the patient must wait at least 12 days beyond the end of her missed 7-day prescription window before her next pregnancy test. This test must be in the first 5 days of her menstrual cycle.

May 2015

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<td>Last day patient may answer their questions More.</td>
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<td>First day of required lockout More.</td>
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</tbody>
</table>

Key:
- Today or future day for an active 7 day window
- A past day for a 7 day window
- A 7 day window that has expired without prescription fill
- Action may occur on this date or any date after

You may click on underlined text to perform the required action.
Patient Program Status as of 6/1/2015 3:59 PM Eastern Time

Name: Jane Smith
Program Status: Qualified to Receive Drug
Action: No prescriber action is required at this time
Expire Date: 6/30/2015 11:59 PM

Information: The patient may fill and pick up their prescription at the pharmacy. The patient must obtain the prescription before 11:59 PM Eastern Time on the last day of the prescription window.
### Re-register Patient

#### Determine Patient Category

**Select Patient Category**

- Patient is a Female of Reproductive Potential (FRP)
- Patient is a Female NOT of Reproductive Potential (FNRP)
- Patient is a Male

**Notice!**

Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your patient's classification. Intentional falsification of Patient classification type will result in permanent Deactivation from the IPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>REVIEW</th>
<th>PREGNANCY RESULT</th>
<th>PATIENT INFO</th>
<th>UNIQUENESS</th>
<th>IDENTIFICATION</th>
<th>FINISH</th>
</tr>
</thead>
</table>

[Cancel] [Continue]
Prescriber - Manage Patients – Re-register Patient Button – Patient linked to a different Prescriber

Re-register Patient

<table>
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<tr>
<th>CATEGORY</th>
<th>REVIEW</th>
<th>PREGNANCY RESULT</th>
<th>PATIENT INFO</th>
<th>UNIQUENESS</th>
<th>IDENTIFICATION #</th>
<th>FINISH</th>
</tr>
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</table>

Determine Patient Category

Select Patient Category

- Patient is a Female of Reproductive Potential (FRP)
- Patient is a Female NOT of Reproductive Potential (FNRP)
- Patient is a Male

Notice!
Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your patient's classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

Cancel  Continue
Re-Register Patient

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>REVIEW</th>
<th>PREGNANCY RESULT</th>
<th>PATIENT INFO</th>
<th>UNIQUENESS</th>
<th>IDENTIFICATION</th>
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</tbody>
</table>

Enter patient information:

- First Name: Jenna
- Last Name: Jones
- Address: 421 Seabrook Road
- City: Blue Bell
- State: PA
- Zip Code: 19034

[Cancel] [Continue]
Prescriber - Manage Patients – Re-register Patient Button – FRP – Patient Information

Re-Register Patient

Enter patient information for Jenna Jones - continued:

<table>
<thead>
<tr>
<th>Category</th>
<th>Review</th>
<th>Pregnancy Result</th>
<th>Patient Info</th>
<th>Uniqueness</th>
<th>Identification</th>
<th>Finish</th>
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</table>

All fields below are required unless otherwise indicated.

Phone: 2105221212

Email: jenna@email.com

Date of Birth (MM/DD/YYYY): 3/7/2000

Last Four Digits of Social Security Number: 7542

Preferred Method of Communication: Email

I have obtained the signed program consent form from the patient.

Cancel  Back  Continue
### Patient Information Review

**Patient Name:** Jenna Jones  
**Address:** 421 Seabrook Road, Blue Bell, PA 19424  
**Phone Number:** 215-522-1212  
**Email:** jenna@email.com  
**Preferred Method of Communication:** Email  
**Date of Birth:** 3/7/2000  
**Last Four Digits of Social Security Number:** 7542

I have obtained the signed program consent form(s) from the patient.
Patient Registration is complete for Jenna Jones. Patient may use their current Patient ID and Password.

This patient has a 30 day wait period before she can be confirmed. This 30 day wait period begins on the date of registration. You may confirm this patient on or after 7/1/2015.

Do not give the patient a prescription to fill until after you provide this confirmation.
Prescriber - Manage Patients – Re-register Patient Button – FNRP – Determine Patient Category

Re-Register Patient

Determine Patient Category:

You have indicated that this patient is a female. The questions that follow will assign a risk category to this female patient, based on her reproductive potential according to the requirements of the iPLEDGE Program.

All female patients are considered Female of Reproductive Potential (FRP) unless one or more of the following applies:

1. Patient has had a hysterectomy
2. Patient has had a bi-lateral oophorectomy
3. Patient is post-menopausal

Please note that the following conditions DO NOT qualify a patient to be moved from the FRP risk category.
- Tubal sterilization
- Partner Vasectomy
- Abstinence
- Patient has not had her first period (pre-menarche)
- Patient is currently in menopause (but not yet post-menopausal)

Please acknowledge your understanding of the qualification criteria as presented to proceed with assigning a risk category to this patient.

Cancel | I Acknowledge

Re-register Patient

Determine Patient Category:

Has patient had a hysterectomy?

- Yes
- No

Notice!

Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient’s classification. Intentional misclassification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of Isotretinoin prescribing privileges.

Cancel  Continue
Re-register Patient

Determine Patient Category:
Has patient had a bilateral oophorectomy?
- Yes
- No

Notice!
Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient's classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

Cancel  Continue
Re-register Patient

Determine Patient Category:

For the iPLEDGE Program, a woman is considered post-menopausal upon cessation of previously occurring menses as a result of ovarian failure with documentation of hormonal deficiency by a certified healthcare provider (e.g. spontaneous menopause).

Hormonal deficiency should be properly documented in the case of spontaneous menopause as follows:

1. If age > 54 years and with the absence of normal menses: Serum FSH (Follicle Stimulating Hormone) level elevated to within the post-menopausal range based on the laboratory reference range where the hormonal assay is performed.

2. If age < 54 years and with the absence of normal menses: Negative serum or urine -hCG with concurrently elevated serum FSH (Follicle Stimulating Hormone) level in the post-menopausal range, depressed estradiol (E2) level in the post-menopausal range, and absent serum progesterone level, based on the laboratory reference ranges where the hormonal assays are performed.

Using the definition above, is this patient post-menopausal?

- Yes
- No

Notice!

Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient’s classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of Isotretinoin prescribing privileges.
### Re-register Patient

**Review Patient Category:**

Based on your responses the iPLEDGE Program system has categorized this patient as follows:

- **Patient is a Female of Reproductive Potential (FRP)**

**Based on the following criteria:**

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
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<tbody>
<tr>
<td>Is patient a Male?</td>
<td>No</td>
</tr>
<tr>
<td>Has patient had a hysterectomy?</td>
<td>No</td>
</tr>
<tr>
<td>Has patient had a bi-lateral oophorectomy?</td>
<td>No</td>
</tr>
<tr>
<td>Is this patient post-menopausal?</td>
<td>No</td>
</tr>
</tbody>
</table>

To confirm the patient category and proceed, click Continue.

To change your responses, click Back.

If your responses are correct, but you still believe this patient to be a Female of NON-Reproductive Potential, click Request FNRP Status.

<table>
<thead>
<tr>
<th>Back</th>
<th>Continue</th>
<th>Request FNRP Status</th>
</tr>
</thead>
</table>
Prescriber - Manage Patients – Re-register Patient Button – Request FNRP Status

Re-Register Patient

Review Patient Category:

Notice!
Your responses indicate that this patient should be registered as a Female of Reproductive Potential (FRP). However, you are requesting to register this patient as a Female NOT of Reproductive Potential (FNRP). This must be due to an unusual circumstance or unique medical condition not covered in the definition of FRP for the iPLEDGE Program.

The following are not reasons to register a patient as an FNRP, and requests based on these reasons will be denied.

- Tubal Sterilization
- Partner Vasectomy
- Abstinence
- Patient has not had her first period (pre-menarche)
- Patient is currently in menopause (but not yet post-menopause)

Please contact the Call Center at 1-866-495-0654 to provide further information. You may be required to provide documentation to support this request.

If this request is denied, the patient will need to be re-registered after a negative pregnancy test. Isotretinoin therapy can only begin 30 days from the date the patient is re-registered.

Back  Continue
Prescriber - Manage Patients – Re-register Patient Button – FNRP – Patient Information

Re-register Patient

Enter patient information:

All fields below are required unless otherwise indicated.

First Name: Jane
Last Name: Smith
Address: 1 Tumble Way
City: Napa
State: MD
Zip Code: 40517

Finish
Cancel Continue

Welcome [DEA# or Unique ID]
Logout

Have Questions? Call our toll-free number 1-866-495-0954
Re-register Patient

Enter patient information for Jane Smith - continued:

- **Phone**: 1231231231
- **Email (Optional)**: email@gmail.com
- **Date Of Birth (MM/DD/YYYY)**: 8/28/1965
- **Last Four Digits Of Social Security Number**: 1968
- **Preferred Method of Communication**: U.S. Mail

☐ I have obtained the signed program consent form from the patient.

[Options: Cancel, Back, Continue]
Re-register Patient

Patient Information Review:

Patient Name: Jane Smith
Address: 123 Test Drive Suite 123 Test City, AL 11122
Phone Number: 123-123-1231
Email: email@email.com
Preferred Method of Communication: U.S. Mail
Date of Birth: 8/28/1968

Last Four Digits of Social Security Number: 1968

I have obtained the signed program consent form from the patient.

Cancel  Back  Continue
Prescriber - Manage Patients – Re-register Patient Button – Request FNRP
Status – Finish

Patient Jane Smith.
Patient may use their current Patient ID and Password.

Registration is not complete until this request for FNRP status is approved by iPLEDGE. This Patient will not be able to start therapy until approved as a FNRP, or until you registered the patient as a PRP.

Please contact the Call Center at 1-866-495-0654 to provide further information. You may be required to provide documentation to support this request.

Select the Finish button to complete this portion of the patient's registration.

Finish
### Re-register Patient

**Determine Patient Category**

- **Select Patient Category**
  - Patient is a Female of Reproductive Potential (FRP)
  - Patient is a Female NOT of Reproductive Potential (FNRP)
  - Patient is a Male

**Notice!**

Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your patient's classification. Intentional misclassification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

[Cancel] [Continue]
Prescriber - Manage Patients – Re-register Patient Button – MALE – Patient Information
Prescriber - Manage Patients – Re-register Patient Button – MALE – Patient Information

Re-register Patient

Enter patient information for John Smith - continued:

All fields below are required unless otherwise indicated.

Phone
1231231231

Email (Optional)
email@email.com

Date Of Birth (MM/DD/YYYY)
8/29/1965

Last Four Digits Of Social Security Number
1989

☐ Check this box if the patient doesn't have a social security number.

Preferred Method of Communication
U.S. Mail

☐ I have obtained the signed program consent form from the patient.

Cancel  Back Continue
Re-register Patient

Patient Information Review:

Patient Name: John Smith
Address: 123 Test Testing, FW 12345
phone Number: 123-123-1231
Email: email@email.com
preferred Method of Communication: U.S. Mail
Date of Birth: 8/28/1968
Last Four Digits of Social Security Number: 1968

I have obtained the signed program consent form from the patient.
Re-Register Patient

Patient Registration is complete for John Smith. Patient may use their current Patient ID and Password.

Before John Smith can fill a prescription, you must confirm patient counseling in the system. Please click the Continue button below to start the confirmation process.

Notice!

Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your patient’s classification. Intentional falsification of patient classification type will result in permanent deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

Otherwise select the Finish button below to complete John Smith’s registration. Note: You may confirm John Smith at a later date using the Manage Patients screen.

Continue

Finish
Prescriber - Manage Patients – Change Patient Type Button – Change to FRP – No PT Results
Change Patient Type

Patient Name: Jane Smith
Patient Type has been changed to: Female of Reproductive Potential (FRP)
Program Status has been changed to: Registered

Patient may use their current Patient ID and Password.

Patient must be given a pregnancy test before beginning a new course of treatment. After a pregnancy test has been administered, return to the Manage Patients screen and select the Complete Change Patient Type button to enter the pregnancy test results. The date the pregnancy test is entered will be the date of registration for the new course of treatment.

Patient must wait at least 30 days after the date of registration before she can start the process for the first prescription. The patient’s next pregnancy test after the 30 day wait is over should be done during the first 5 days of her menstrual period.

Remind this patient to use two methods of contraception.

Finish
Prescriber - Manage Patients – Change Patient Type Button – Change to FRP – Negative Pregnancy Test Results
Prescriber - Manage Patients – Change Patient Type Button – Change to FRP – Negative PT Results – Finish

Patient Name: Jane Smith
Patient Type has been changed to: Female of Reproductive Potential (FRP)
Program Status has been changed to: Registered

Patient may use their current Patient ID and Password
A new course of treatment has been initiated. This patient has a 30 day wait period before she can be confirmed. You may confirm this patient on or after 7/1/2015.
A second pregnancy test is required when the patient is confirmed.
For patients with regular menstrual cycles, the second pregnancy test should be done during the first 5 days of the menstrual period immediately preceding the beginning of isotretinoin therapy, and after the patient has used 2 methods of contraception for 1 month.
For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 methods of contraception for 1 month.

Finish
Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP
Prescriber - Manage Patients – Change Patient Type Button – Change to FNRPR – Determine Patient Category

**Change Patient Type**

**Determine Patient Category:**

You have indicated that this patient is a female. The questions that follow will assign a risk category to this female patient, based on her reproductive potential according to the requirements of the iPLEDGE Program.

All female patients are considered Female of Reproductive Potential (FRP) unless one or more of the following applies:

1. Patient has had a hysterectomy
2. Patient has had a bilateral oophorectomy
3. Patient is post-menopausal

Please note that the following conditions DO NOT qualify a patient to be moved from the FRP risk category:

- Tubal Sterilization
- Male Vasectomy
- Abstinence
- Patient has not had her first period (pre-menarche)
- Patient is currently menopausal (but not yet post-menopausal)

Please acknowledge your understanding of the qualification criteria as presented to proceed with assigning a risk category to this patient.
Determine Patient Category:

Has patient had a hysterectomy?

- Yes
- No

Notice!
Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your patient's classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.
Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category – Question 2 of 3

Notice!
Make sure that you are correctly classifying your patient as you may be required to provide documentation to support your Patient's classification. Intentional falsification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of Isotretinoin prescribing privileges.
Determine Patient Category:

For the iPLEDGE Program, a woman is considered post-menopausal upon cessation of previously occurring menses as a result of ovarian failure with documentation of hormonal deficiency by a certified healthcare provider (i.e. spontaneous menopause).

Hormonal deficiency should be properly documented in the case of spontaneous menopause as follows:

1. If age > 54 years and with the absence of normal menses: Serum FSH (Follicle Stimulating Hormone) level elevated to within the post-menopausal range based on the laboratory reference range where the hormonal assay is performed.

2. If age < 54 years and with the absence of normal menses: Negative serum or urine hCG with concurrently elevated serum FSH (Follicle Stimulating Hormone) level in the post-menopausal range, depressed estradiol (E2) level in the post-menopausal range, and absent serum progesterone level, based on the laboratory reference ranges where the hormonal assays are performed.

Using the definition above, is this patient post-menopausal?

- Yes
- No

Notice!

Make sure you are correctly classifying your patient as you may be required to provide documentation to support your Patient's classification. Incorrect classification of Patient classification type will result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privileges.

Cancel  Continue
Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category – Review

Change Patient Type

Review Patient Category:
Based on your responses the iPledge Program system has categorized this patient as follows:
Patient is a Female of Reproductive Potential (FRP)

Based on the following criteria:
- Has patient had a hysterectomy? No
- Has patient had a bilateral oophorectomy? No
- Is this patient post-menopause? No

To confirm the patient category and proceed, click Continue.
To change your responses, click Back.
If your responses are correct, but you still believe this patient to be a Female of NON-Reproductive Potential, click Request FNRP Status

Back  Continue  Request FNRP Status
Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category – Review

Notice!

Your responses indicate that the patient should be registered as a Female of Reproductive Potential (FPRP). However, you are requesting to register the patient as a Female NOT of Reproductive Potential (FNRP). This must be due to an unusual circumstance or unique medical condition not covered in the definition of FNRP for the iPLEDGE Program.

The following are Not reasons to register a patient as an FNRP, and requests based on these reasons will be denied:

- Tubal Sterilization
- Male Vasectomy
- Abstinence
  - Patient has not had her first period (pre-menarche)
  - Patient is currently in menopause (but not yet post-menopausal)

Please contact the Call Center at 1-866-465-0654 to provide further information. You may be required to provide documentation to support this request.

If this request is denied, the patient will need to be re-registered after a negative pregnancy test. Isotretinoin therapy can only begin 30 days from the date the patient is re-registered.
Prescriber - Manage Patients – Change Patient Type Button – Change to FNRP – Determine Patient Category – Request FNRP

**Notice!**
Your responses indicate that the patient should be registered as a Female of Reproductive Potential (FRP). However, you are requesting to register this patient as a Female NOT of Reproductive Potential (FNRP). This must be due to an unusual circumstance or unique medical condition not covered in the definition of FNRP for the iPLEDGE Program.

The following are not reasons to register a patient as an FNRP, and requests based on these reasons will be denied.

- Tubal Sterilization
- Male Vasectomy
- Abstinence
- Male patient has not had his first period (pre-menarche)
- Male patient is currently in menopause (but not yet post-menopause)

Please contact the Call Center at 1-866-495-6654 to provide further information. You may be required to provide documentation to support this request.

If this request is denied, the patient will need to be re-registered after a negative pregnancy test. Testosterone therapy can only begin 30 days from the date the patient is re-registered.

**Back**  **Continue**
Re-register Patient

Patient Jane Smith.
Patient may use their current Patient ID and Password.

Registration is not complete until the request for FNRP status is approved by the iPLEDGE Program. This patient will not be able to start therapy until approved as a FNRP, or until you register the patient as an FRP.

Please contact the Call Center at 1-866-495-0654 to provide further information. You may be required to provide documentation to support this request.

Select the Finish button to complete this portion of the patient’s registration.
Prescriber - Manage Patients – Discontinue Patient Button – Discontinue Reasons

Discontinue Patient

All fields below are required unless otherwise indicated.

Patient ID: 3011101093
First Name: Jane
Last Name: Smith
Date of Birth: 11/10/1983

The iPLEDGE Program system has no record of a prescription being filed for this patient. Do you believe this patient has taken isotretinoin during this course of therapy?

- Yes
- No
- Not Sure

Discontinue Reason:
- Patient Completed Therapy
- Patient is Lost to Follow Up
- Pregnancy
- Patient has Insurance Considerations
- Patient Never Started Therapy
- Other

Cancel  Continue
Prescriber - Manage Patients – Report Pregnancy Button

Report Pregnancy

Identification Number: 3304181997
First Name: Jane
Last Name: Smith
Date of Birth: 04/18/1997
Current Program Status: Registered

Enter the Specimen Collection Date:
May / 28 / 2015

Cancel Continue
Prescriber - Manage Patients – Report Pregnancy Button: 1 of 3

Report Pregnancy

Identification Number: 3304191997
First Name: Jane
Last Name: Smith
Date of Birth: 04/18/1997
Current Program Status: Registered

Confirm the Specimen Collection Date:
Specimen Collection Date you entered is: 5/28/2015

Confirm the Specimen Collection Date

Pregnancy Test Type:
- Select
- Quantitative Serum
- Qualitative Serum
- Urine
- Positive

Prescriber Diagnosis:
Pregnant

You are reporting this patient pregnant.
To enter this patient’s monthly pregnancy results, please use the Confirm Patient Counseling feature found on the Manage Patients screen.

Back Report Patient Pregnant

Reference ID: 4252185
Prescriber - Manage Patients – Report Pregnancy Button: 2 of 3

Report Pregnancy

Identification Number: 3304181997
First Name: Jane
Last Name: Smith
Date of Birth: 04/10/1997
Current Program Status: Registered

Confirm the Specimen Collection Date:
Specimen Collection Date you entered is: 5/28/2015

Confirm the Specimen Collection Date

Pregnancy Test Type: Select

Lab Test Results:
Positive
Negative
Non-Pregnancy

You are reporting this patient pregnant.
To enter this patient’s monthly pregnancy results, please use the Confirm Patient Counseling feature found on the Manage Patients screen.

Back Report Patient Pregnant

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Prescriber - Manage Patients – Report Pregnancy Button – Confirmation
Prescriber - Order Materials

Order Materials

Enter quantities you would like to order

0 iPLEDGE Program Birth Control Information Sheet iPLEDGE Program Checklist (1 to 10 sheets)
0 Prescribing checklist for Female Patients of Reproductive Potential (1 to 3 packs of 50 tear sheets)
0 Prescribing checklist for Male Patients and Female Patients of Non-Reproductive Potential (1 to 3 packs of 50 tear sheets)
0 Educational DVDs: Be Prepared, Be Protected and Be Aware: The Risk of Pregnancy while on Isotretinoin (1 DVD)
0 Patient Introductory Brochure (1 to 3 packages of 5)
0 Isotretinoin Educational Kit for Female Patients Who Can Get Pregnant (1 to 10 kits)
0 Isotretinoin Educational Kit for Male Patients and Female Patients Who Cannot Get Pregnant (1 to 10 kits)
0 Prescriber Isotretinoin Educational Kit (1 Kit)
0 Spanish Patient Introductory Brochure (1 to 3 packages of 5)
0 Spanish Isotretinoin Educational Kit for Female Patients Who Can Get Pregnant (1 to 10 kits)
0 Spanish Isotretinoin Educational Kit for Male Patients and Female Patients Who Cannot Get Pregnant (1 to 10 kits)

Place Order
Prescriber - Update My Information – Change Password

Change Password

All fields below are required unless otherwise indicated.

Old Password

New Password

Confirm New Password

Save Changes
Change Date of Personal Significance

Your Date of Personal Significance is a date that you will be able to remember (such as an anniversary) and will be used to verify your identity if you need to contact the Call Center.

All fields below are required unless otherwise indicated.

Password

Date of Personal Significance: (MM/DD/YYYY)

Confirm Date of Personal Significance: (MM/DD/YYYY)

Save Changes
Prescriber - Update My Information – Contact Info

Update Contact Information

Use this form to edit your contact information. Enter or confirm your information. All fields below are required unless otherwise indicated.

First Name

MI (Optional) Suffix (Optional)

Last Name

Specialty (Optional)

Practice Name (Optional)

Address

City

State Zip

Preferred/Method of Communication

Phone Number Ext (Optional)

Email (Optional)

Fax Number (Optional)

Prescriber Identifiers

This notification is to inform you that with the launch of the REMS Pharmacy Network, the iPLEDGE Program will require prescribers to provide a National Provider Identifier (NPI). If your NPI is not on file with the iPLEDGE Program, you will be prompted to enter your NPI upon first log-in to the enhanced iPLEDGE Program. Additionally, if you are registered with the Drug Enforcement Administration (DEA), the system will require entry of your DEA number. Failure to supply these identifiers may result in your patient's prescriptions not being authorized for dispensing.

DEA

NPI

I do not have a DEA

Cancel Save Changes

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Reference ID: 4252185
Required Information Request

Due to system enhancements, additional information is required. Please review and verify that your information is correct.

Continue

Required Information Missing
Prescriber - Manage Delegates/Designees

Manage Delegates and Designees

Delegates

A prescriber can delegate another registered and activated PLEDGE Program prescriber to cover for him/her during a scheduled absence (travel, vacation, etc.). This also can be used to delegate to another registered and activated prescriber in a multiple doctor practice where a patient may see any of the doctors in the office. Delegate status has an expiration date that can be set by the delegating prescriber.

Designees

A designee is a staff member in the prescriber’s office. A registered designee may perform all patient functions on behalf of the prescriber. An office designee may support all the registered prescribers in a multi-physicians practice and will also have rights for any patient of a delegate prescriber. Each office staff designee will only need to register once, even if they support several prescribers. Also, if a prescriber is not activated in the PLEDGE program system, neither the prescriber nor the designated office staff can register a patient. The registered prescriber is responsible for all information entered and activities performed in the PLEDGE Program by all designees under his/her supervision.
Prescriber - Manage Delegates

Manage Delegates

Delegates are prescribers that are registered and activated in the iPLEDGE program that you allow to manage your patients.

- To add a delegate, click on the Add Delegate button.
- To remove a delegate, select Remove from the Action drop down and click on the Go button.
- To update a delegate, select Update from the Action drop down and click on the Go button.

Select the appropriate action from the Actions drop down within the applicable delegate row and click Go to perform the action.

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>User Name</th>
<th>Expiration Date</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stephen</td>
<td>Cox</td>
<td>AC1324568</td>
<td>No Exp Data</td>
<td>Remove</td>
</tr>
</tbody>
</table>

Showing 1 to 1 of 1 entries

Add Delegate
### Manage Designees

Designees are office staff that are registered in the iPLEDGE Program that you allow to manage your patients.

**Note:** The registered prescriber is responsible for all information entered and activities performed in the iPLEDGE Program by all designees under their supervision.

- To add a designee, click on the Add Designee button.
- To remove a designee, select Remove from the Actions drop down and click on the Go button.

Select the appropriate action from the Actions drop down within the applicable delegate row and click Go to perform the action.

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>User Name</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shalu</td>
<td>Designee</td>
<td>542098155</td>
<td>--Select-- Go</td>
</tr>
<tr>
<td>Test</td>
<td>Designee</td>
<td>547555740</td>
<td>--Select-- Go</td>
</tr>
<tr>
<td>DesigneeTestOne</td>
<td>DesigneeTestOne</td>
<td>547749252</td>
<td>--Select-- Go</td>
</tr>
<tr>
<td>DesigneeTestTwo</td>
<td>DesigneeTestTwo</td>
<td>547749463</td>
<td>--Select-- Go</td>
</tr>
<tr>
<td>JASON</td>
<td>KOCH</td>
<td>542342074</td>
<td>--Select-- Go</td>
</tr>
<tr>
<td>Vivek</td>
<td>spurthi</td>
<td>542342230</td>
<td>--Select-- Go</td>
</tr>
<tr>
<td>Vivek</td>
<td>spurthi</td>
<td>542999494</td>
<td>--Select-- Go</td>
</tr>
</tbody>
</table>

Showing 1 to 7 of 7 entries

Add Designee
**Prescriber Program Status**

Your Program Status: Attested
Program Status expiration date: 5/28/2015

<table>
<thead>
<tr>
<th>Full Name</th>
<th>Phone</th>
<th>Date of Birth</th>
<th>Type</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRP, Female</td>
<td>123-123-1231</td>
<td>10/20/1970</td>
<td>Patient FRP</td>
<td>Active</td>
</tr>
<tr>
<td>gtest, Test 2</td>
<td>222-222-2222</td>
<td>08/29/1969</td>
<td>Patient FRP</td>
<td>Active</td>
</tr>
<tr>
<td>Jones, Jenna</td>
<td>215-522-1212</td>
<td>03/07/2000</td>
<td>Patient FRP</td>
<td>Active</td>
</tr>
<tr>
<td>kyesyl, klest1</td>
<td>999-999-9999</td>
<td>01/01/1940</td>
<td>Patient FRP</td>
<td>Permanently Lost to Follow Up</td>
</tr>
<tr>
<td>Patient, FRP</td>
<td>123-123-1231</td>
<td>10/21/1921</td>
<td>Patient FRP</td>
<td>Permanently Lost to Follow Up</td>
</tr>
<tr>
<td>Patient, FRP</td>
<td>555-555-1212</td>
<td>11/10/1991</td>
<td>Patient FRP</td>
<td>Permanently Lost to Follow Up</td>
</tr>
<tr>
<td>Patient, FRP</td>
<td>555-555-1212</td>
<td>11/10/1993</td>
<td>Patient FRP</td>
<td>Permanently Lost to Follow Up</td>
</tr>
<tr>
<td>Patient, Male</td>
<td>123-123-1231</td>
<td>08/28/1968</td>
<td>Patient FNRP</td>
<td>Inactive</td>
</tr>
</tbody>
</table>

Showing 1 to 8 of 8 entries

1 » 10
Frequently Asked Questions (FAQ)

iPLEDGE PROGRAM (click topics below for more information)

A. TECHNICAL ASSISTANCE
B. PRESCRIBER
C. ALL USERS
### Action Required List

Based on the iPLEDGE Program requirements, listed below are actions that are required. Please provide the required information to ensure completion of all iPLEDGE Program requirements.

<table>
<thead>
<tr>
<th>Name</th>
<th>Message</th>
<th>Take Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown, Cindy 3301822099</td>
<td>Enter the initial post-therapy Pregnancy Test Results, due upon completion of therapy.</td>
<td></td>
</tr>
<tr>
<td>Brown, Sandy 3301692000</td>
<td>One or both post-therapy Pregnancy Test Results due upon completion of therapy (at completion and 30 days after completion of therapy) have not been entered into iPLEDGE. The Patient program status will change to Permanently Lost To Follow Up on 01/07/2010 if post-therapy Pregnancy Test Results are not entered.</td>
<td></td>
</tr>
<tr>
<td>Dough, Jane 3304941964</td>
<td>Patient has been in “Registered” status for over 60 days. If no activity occurs, the system will discontinue this patient on 01/03/2010.</td>
<td></td>
</tr>
<tr>
<td>Patient, FCP 3316971967</td>
<td>Post-therapy Pregnancy Test Results are required at completion of therapy and 30 days after completion of therapy. One or both of these post therapy Pregnancy Test Results are now due.</td>
<td></td>
</tr>
<tr>
<td>Patient, T 3201641964</td>
<td>During registration, this patient was determined to be a female of reproductive potential (FRP). However, you have requested to register this patient as a female not of reproductive potential (FNRP). Please contact the Call Center to discuss reasons for this request and complete this patient’s registration.</td>
<td></td>
</tr>
</tbody>
</table>

Showing 1 to 5 of 5 entries

1 > 10
iPLEDGE Privacy Notice and Terms of Use

Version 2.0, Last Revised: 09/17/2015

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These Terms of Use are between a user of any portion of the Site (“you” or “your”) and the sponsors of the Site (“iPLEDGE” “we”, “us” and “our”).

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UPDATES
IPLIDGE
Committed to Pregnancy Prevention

Welcome
Have Questions? Call our toll-free number 1-888-495-0854

HOME
PATIENT INFORMATION
ABOUT ISOTRETINOIN
ABOUT IPLIDGE
PRESCRIBER INFORMATION
FIND A PARTICIPATING PHARMACY
FAQS

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This program is called IPLIDGE®. Under this program, prescribers must be registered and activated with the IPLIDGE Program and can prescribe isotretinoin only to registered patients who meet all the requirements of IPLIDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with IPLIDGE. Registered and activated pharmacies can only receive isotretinoin from wholesalers registered with IPLIDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurting themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking tetracycline. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lips, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with isotretinoin.

Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.
FDA REMS Submission

Public and Common Screens Inventory

iPLEDGE Program

Revised: December 2017
Public and Common Screens Inventory:

**Table of Contents**

<table>
<thead>
<tr>
<th>Public Home Page</th>
<th>..........................................................</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program Update Box</td>
<td>...............................................................................</td>
<td>4</td>
</tr>
<tr>
<td>Office Staff Designee Registration</td>
<td>..................................................................................</td>
<td>5</td>
</tr>
<tr>
<td>Common – Patient Information</td>
<td>.................................................................................</td>
<td>6</td>
</tr>
<tr>
<td>Common – About Isotretinoin</td>
<td>.....................................................................................</td>
<td>7</td>
</tr>
<tr>
<td>Common – About iPLEDGE</td>
<td>.......................................................................................</td>
<td>8</td>
</tr>
<tr>
<td>Public – Prescriber Information</td>
<td>..................................................................................</td>
<td>9</td>
</tr>
<tr>
<td>Public – Find a Participating Pharmacy</td>
<td>................................................................................</td>
<td>10</td>
</tr>
<tr>
<td>Public – FAQs</td>
<td>..................................................................................</td>
<td>11</td>
</tr>
<tr>
<td>Common – iPLEDGE Terms of Use</td>
<td>................................................................................</td>
<td>12</td>
</tr>
<tr>
<td>Common – Safety Notice</td>
<td>..................................................................................</td>
<td>13</td>
</tr>
<tr>
<td>Public – Forgot Password</td>
<td>..................................................................................</td>
<td>14</td>
</tr>
<tr>
<td>User login timed out</td>
<td>..................................................................................</td>
<td>15</td>
</tr>
</tbody>
</table>
SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking Isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, Isotretinoin can only be marketed under a special restricted distribution program. This program is called IPLEDGE®. Under this program, prescribers must be registered and activated with the IPLEDGE Program and can prescribe Isotretinoin only to registered patients who meet all the requirements of PLEDGE. Isotretinoin can be dispensed only by a pharmacy registered and activated with PLEDGE. Registered and activated pharmacies can only receive Isotretinoin from wholesalers registered with IPLEDGE.

Patients on isotretinoin have been known to become depressed or to develop other serious mental health problems. Some people have had thoughts of hurtling themselves or putting an end to their own lives. Some people tried to end their own lives and some have ended their own lives. There have been reports that people on isotretinoin were aggressive or violent. No one knows if isotretinoin caused these problems or behaviors or if they would have happened even if the person did not take isotretinoin.

Isotretinoin use has been associated with pseudotumor cerebri, a condition caused by increased pressure on the brain. This condition may occur more often in patients also taking birth control pills. Patients should be aware of other serious side effects, including problems with the skin, pancreas, liver, stomach, bones, muscles, hearing, vision, lips, allergic reactions, blood sugar, or red and white blood cells. The most common, less serious adverse events include dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Patients should be advised about these adverse events and routinely monitored by a doctor during treatment with Isotretinoin.

Please refer to the Isotretinoin package insert for full prescribing and dispensing instructions.

Registration

Patient Information

Pharmacy Registration

Prescriber Registration

Office Staff Designer Information

How to Report

Call our toll free number 1-866-495-9654 to report any of the following:

An Adverse Event: If you or someone you know has experienced an adverse event, please call 1-866-495-9654.

A Pregnancy: If you are an activated prescriber, report pregnancy results by logging in and clicking on “Manage Patients.” Otherwise, please call 1-866-495-9654.
Office Staff Designee Registration

Office Staff Designee cannot register directly in the iPLEDGE Program. All Designees must be registered in the iPLEDGE Program by a Prescriber. A Prescriber is a medical professional such as a doctor, physician assistant, or nurse practitioner who has prescribing privileges. If you believe you should be registered in the iPLEDGE Program as a Designee, please discuss with your sponsoring Prescriber.
Common – Patient Information

Patient Information

About Patient Information
Are you thinking about starting treatment with isotretinoin? You can learn more about isotretinoin and about the iPLEDGE Program by reading the introductory information brochure and the medication guide available below.

View Information Online
You can click on each link to view the material online. Upon clicking on a link, each file will be launched in a new browser window. To view these PDF files, you will need Acrobat Reader®.

Patient Information:
- Patient Introductory Brochure
- Dr. Reddy’s Zenafide Medication Guide
- Mylan Amnesteem Medication Guide
- Sun Aironia Medication Guide
- Teva Claravis Medication Guide
- Airon Myorisan Medication Guide
- Amneal Isotretinoin Medication Guide

Manufacturers’ Toll-free Numbers
For more information about the specific brands of isotretinoin, call the individual manufacturers at these numbers.

<table>
<thead>
<tr>
<th>Product Name</th>
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<td>Mylan Pharmaceuticals Inc.</td>
<td>1.800.796.9526</td>
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<tr>
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<td>Teva Pharmaceuticals USA, Inc.</td>
<td>1.800.227.7522</td>
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<td>Airon, Inc.</td>
<td>1.877.254.4381</td>
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<td>Zenafide™</td>
<td>Dr. Reddy’s Laboratories, Ltd.</td>
<td>1.888.375.3784</td>
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<tr>
<td>Amneal Isotretinon</td>
<td>Amneal Pharmaceuticals, LLC</td>
<td>1.877.835.5472</td>
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About Isotretinoin

CONTRAINDICATIONS AND WARNINGS
Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 65 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, microtia, small or absent external auditory canals); eye abnormalities (including microphthalmia and facial dysmorphia); cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebellar abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements
Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPledge®. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPledge Program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPledge, and must only be dispensed to patients who are registered and meet all the requirements of iPledge.
Common – About iPLEDGE

About iPLEDGE

The iPLEDGE Program is a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the FDA. The program strives to ensure that:

- No female patient starts isotretinoin therapy if pregnant
- No female patient on isotretinoin therapy becomes pregnant

This enhanced program is a SINGLE pregnancy risk management program for prescribing and dispensing all isotretinoin products (brand and generic products). The iPLEDGE Program requires registration of all wholesalers distributing isotretinoin, all healthcare professionals prescribing isotretinoin, all pharmacies dispensing isotretinoin, and all male and female patients prescribed isotretinoin. This program is designed to create a verifiable link between the negative pregnancy test and the dispensing of the isotretinoin prescription to the female patient of reproductive potential. The iPLEDGE Program requires that all patients meet qualification criteria and monthly program requirements. Before the patient receives his/her isotretinoin prescription each month, the prescriber must counsel the patient and document in the iPLEDGE Program system that the patient has been counseled about the risks of isotretinoin.

There are also additional qualification criteria and monthly requirements for female patients of reproductive potential.

As part of the ongoing risk management of isotretinoin products, it is crucial that a female of reproductive potential selects and commits to use two methods of effective contraception simultaneously for one month before, during, and for one month after isotretinoin therapy. She must have 2 negative urine or blood (serum) pregnancy tests with a sensitivity of at least 25 mIU/ml before receiving the initial isotretinoin prescription. The first pregnancy test is a screening test and can be conducted in the prescriber’s office. The second pregnancy test must be done in a CLIA-certified laboratory according to the package insert. Each month of therapy, the patient must have a negative result from a urine or blood (serum) pregnancy test conducted by a CLIA-certified laboratory prior to receiving each prescription.

Each month, the prescriber must enter the female patient’s pregnancy results and the 2 methods of contraception she has been using in the iPLEDGE Program system. The iPLEDGE Program system verifies that all criteria have been met by the prescriber, patient, and pharmacy prior to granting the pharmacy authorization to fill and dispense isotretinoin. The pharmacist must obtain authorization from the iPLEDGE Program system via the internet (www.ipledgeprogram.com), telephone (1-866-495-0654) or through electronic telecommunication verification (via submission of an isotretinoin prescription claim) prior to dispensing each isotretinoin prescription for both male and female patients.
Public – Prescriber Information

Prescriber Information

About Prescriber Information
The goals of the PLEDGE Program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin’s serious risks and safe-use conditions. The resources below present the program requirements and help you prepare and plan treatments with patients during the course of isotretinoin therapy.

View Information Online
You can click on each link to view the material online. Upon clicking on a link, each file will be launched in a new browser window. To view these PDF files, you will need Acrobat Reader.

Prescriber Information:
- Patient Introductory Brochure
- Prescriber Isotretinoin Educational Kit
- Dr. Reddy’s Zenatane Package Insert
- Mylan Amnesteem Package Insert
- Sun Apretica Package Insert
- Teva Claravis Package Insert
- Akorn Myorisan Package Insert
- Amneal isotretinoin Package Insert

Lessons Learned:
- About Leftover Medication
- About Birth Control
- About Post-Treatment Pregnancy Testing

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iPLEDGE Privacy Notice and Terms of Use

Version 2.0. Last Revised: 08/17/2015

These Terms of Use apply to all visitors of the prescription drug risk management site located at http://www.ipledgeprogram.com (the “Site”). The “iPLEDGE Website” is a Registered User-only account portal available through the site which enables Registered Users to participate in a computer-based risk management program designed to further the public health goal to eliminate fetal exposure to isotretinoin through a special restricted distribution program approved by the FDA.

THIS SITE IS INTENDED FOR U.S. AUDIENCES ONLY. USERS WHO ACCESS THE SITE FROM OUTSIDE THE U.S. DO SO AT THEIR OWN INITIATIVE AND RISK AND ARE RESPONSIBLE FOR COMPLIANCE WITH ALL APPLICABLE LAWS.

“Registered Users” include Patients, Prescribers, Designated Agents, and Pharmacists who have signed up to participate in the iPLEDGE Program. “Patients” are patients that have been prescribed restricted distribution drugs pursuant to the iPLEDGE Program. “Prescribers” are prescribers that prescribe restricted distribution drugs pursuant to the iPLEDGE Program. “Designated Agents” are persons designated by Prescribers to act on their behalf with the iPLEDGE Website. Pharmacists are pharmacists that utilize the iPLEDGE Website to verify a patient's enrollment in the iPLEDGE and status before filling a prescription at a retail pharmacy.

These Terms of Use are between a user of any portion of the Site ("you" or "your") and the sponsors of the Site ("iPLEDGE" “we,” “us” and “our”).

REGISTRATION AND ASSENT
Access to and use of the Site is conditioned upon your assent to these Terms of Use. You are deemed to have assented to these Terms of Use when you use any available page of the Site. You are deemed to have assented to these Terms of Use as applicable to the iPLEDGE Website, when you complete the online registration processes required for Registered Users and indicate during the registration process that you accept these Terms of Use along with the Privacy Policy incorporated therein. You are deemed to have accepted these Terms of Use each time you access the Site and each time you use your login credentials to access the iPLEDGE Website portion of the Site. By registering for or otherwise accessing or using the Site, you acknowledge that you have read, understand, and agree to be legally bound by these Terms of Use. These Terms of Use and the Privacy Policy are available during registration for the iPLEDGE Website and on various pages of the Site.

UPDATES

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SAFETY NOTICE

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Please refer to the isotretinoin package inserts for full prescribing and dispensing instructions.
User login timed out
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

TATIANA OUSSOVA
04/23/2018