

Initial REMS Approval: 10/2010  
Most Recent Modification: April 2018



**iPLEDGE**<sup>®</sup>  
Committed to Pregnancy Prevention

The iPLEDGE Program



# Pharmacist Guide

The resource to help the pharmacist understand and comply with the iPLEDGE Program for 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* 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 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 the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program (see PRECAUTIONS).



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## 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.

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

## 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.<sup>1</sup> 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.

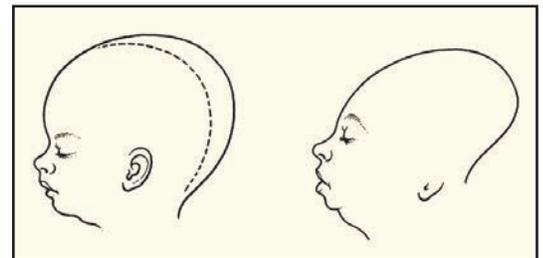
## Birth Defects

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

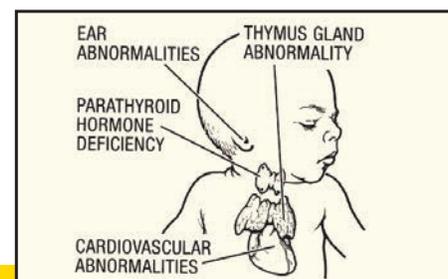
Skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphism; cleft palate.



Line drawing represents the possible abnormalities of the low-set, deformed, or absent ears; wide-set eyes; depressed bridge of nose; enlarged head; and small chin.

### 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.



Line drawing represents the possible abnormalities of the brain, heart, and thymus gland that may occur.

## 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.

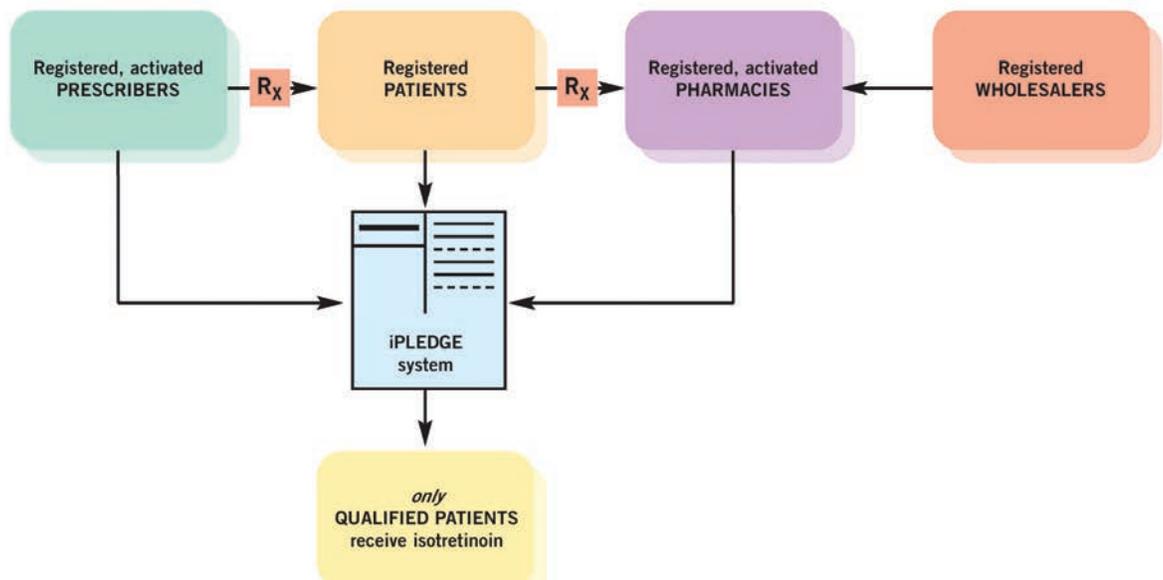
The iPLEDGE Program is a single, shared Risk Evaluation and Mitigation Strategy (REMS) program with requirements for prescribers, pharmacies, patients, and wholesalers. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

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



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 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.

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

## 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.



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



- 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](http://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](http://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)



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

## 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.

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

## 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.



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

- 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](http://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<sup>®</sup> 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.



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

## 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.



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

- 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.



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

## 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

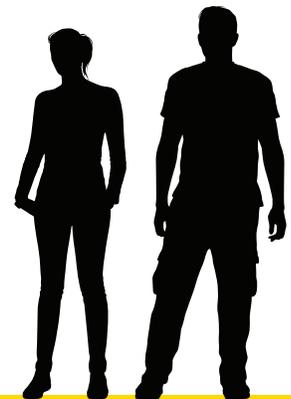
The following section covers general aspects of the iPLEDGE Program.

### 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.



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



**Choose 1 Primary + 1 Secondary Birth Control Method**

Primary Method of Birth Control (Choose One)*	How to Use it	<b>MORE EFFECTIVE</b>	How Well it Works	Benefits†	Risks‡
<b>Hormonal Implant</b> 	Placed under skin of arm by a clinician. Works for 3 years. <sup>1</sup>		>99% <sup>1</sup>	<ul style="list-style-type: none"> <li>Nothing to do or remember</li> <li>Light or no periods</li> <li>May decrease acne</li> <li>No increased risk of clots</li> </ul>	• Irregular Periods
<b>Hormonal IUD</b> 	Placed in uterus by clinician. Self-check monthly. Works for 5 years. <sup>1</sup>		>99% <sup>1</sup>	<ul style="list-style-type: none"> <li>Light or no periods</li> <li>No increased risk of clots</li> </ul>	• Irregular Periods
<b>Non-Hormonal IUD</b> 	Placed in uterus by a clinician. Self-check monthly. Works for 10 years. <sup>3</sup>		>99% <sup>1</sup>	<ul style="list-style-type: none"> <li>No hormones</li> <li>Periods remain regular</li> <li>Effective immediately</li> <li>No increased risk of clots</li> </ul>	• May cause heavier periods and cramping
<b>Tubal Sterilization</b> 	Surgical procedure to close the tubes between the uterus and the ovaries.		>99% <sup>2</sup>	<ul style="list-style-type: none"> <li>It is a virtually permanent method of birth control</li> <li>Nothing to do or remember</li> </ul>	• If you want to have child later, it is very difficult to re-open the tubes
<b>Male Vasectomy</b> 	Surgical procedure that closes off the tubes that carry a partner's sperm.		>99% <sup>2</sup>	<ul style="list-style-type: none"> <li>It is a virtually permanent method of birth control</li> <li>Nothing to do or remember</li> </ul>	• If you want to have child later, it is very difficult to re-open the tubes
<b>Hormonal Shot</b> 	Given every 3 months by a clinician.		>97% <sup>1</sup>	<ul style="list-style-type: none"> <li>Light or no periods</li> <li>No increased risk of clots</li> </ul>	<ul style="list-style-type: none"> <li>Irregular Periods</li> <li>May cause weight gain</li> </ul>
<b>Vaginal Ring</b> 	You place in vagina. Replace monthly.		92% <sup>1</sup>	<ul style="list-style-type: none"> <li>Lighter periods</li> <li>May decrease acne</li> </ul>	• Blood clots
<b>Hormonal Patch</b> 	You place on skin. Replace weekly.		92% <sup>1</sup>	<ul style="list-style-type: none"> <li>Lighter periods</li> <li>May decrease acne</li> </ul>	• Blood clots
<b>Birth Control Pill (Combination Type)</b> 	Swallow at the same time daily.		92% <sup>1</sup>	<ul style="list-style-type: none"> <li>Lighter periods</li> <li>May decrease acne</li> </ul>	• Blood clots

Secondary Method of Birth Control (Choose One)	How to Use it	Benefits	Risks
<b>Condoms</b> (with or without spermicide)	Partner must be willing to use each and every time you have sex.	<ul style="list-style-type: none"> <li>Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS</li> </ul>	• Allergic Reactions
<b>Cervical Cap, Diaphragm</b> (must be used with spermicide). <b>Vaginal Sponge</b>	Place in vagina before you have sex.	<ul style="list-style-type: none"> <li>You are in control of its use</li> </ul>	• Allergic Reactions

\*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.

‡All pictograms from FDA website [www.fda.gov/downloads/forconsumers/byaudience/forwomen/freepublications/ucm356451.pdf](http://www.fda.gov/downloads/forconsumers/byaudience/forwomen/freepublications/ucm356451.pdf). Accessed January 20, 2016.

References 1. Werner CA, Papic MJ, Ferris LK, Schwartz EB. Promoting safe use of isotretinoin by increasing contraceptive knowledge. *JAMA Dermatol.* 2015;151(4):389-393. 2. Trussell J. Contraception failure in the United States. *Contraception.* 2011;83:397-404. Available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3638209/>. Accessed September 9, 2014. 3. ParaGard® Prescribing Information, Teva Women's Health, Inc., June 2013.

## 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.

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

## 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](http://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.**

<p>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:</p>	
<p><b>Female patients who can get pregnant</b></p>	<p><b>Male patients and female patients who cannot get pregnant</b></p>
<p>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.</p> <p>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.</p>	<p>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.</p> <p>To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit.</p>
<p>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.*</p>	

\*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.



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



## 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](http://www.ipledgeprogram.com)**.

### Reference

1. Dai WS, Hsu M-A, Itri LM. Safety of pregnancy after discontinuation of isotretinoin. *Arch Dermatol*. 1989;125:362-355.





**iPLEDGE**<sup>®</sup>  
Committed to Pregnancy Prevention

## For iPLEDGE Program Information

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



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Committed to Pregnancy Prevention



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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 – Pharmacy Registration – For Responsible Site Pharmacists (Button) from Public Home Page



**iPLEDGE**  
Committed to Pregnancy Prevention

Welcome [NCPDP#]  
[Logout](#)

Have Questions? Call our toll-free number 1-866-495-0654

THE ONLY WAY

**HOME**

**ACTIVATE PHARMACY  
REGISTRATION**

**PHARMACY INFORMATION**

**ABOUT ISOTRETINOIN**

**ABOUT iPLEDGE**

**FILL PRESCRIPTION**

**REVERSE PRESCRIPTION**

**FIND WHOLESALER**

**MY PROGRAM STATUS**

**ORDER MATERIALS**

**UPDATE MY INFORMATION**

**FIND A PARTICIPATING  
PHARMACY**

**FAQS**

## 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

**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

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

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

Phone Number

Ext (Optional)

Email (Optional)

Fax (Optional)

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Can your pharmacy management system adjudicate claims?

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Save and Print



**iPLEDGE®**

Committed to Pregnancy Prevention

Have Questions? Call our toll-free number **1-866-495-0654**

## Pharmacy Registration

**Mail To**

iPLEDGE - Committed to Pregnancy Prevention  
PO BOX 2904  
Pheonix AZ 85038-9978

**Or Fax to**

1-866-495-0660

**Username**

2031543T

**Your Information:**

Male Brevik  
7510 East Camelback Road  
Scottsdale, AZ 85251  
Phone 602-819-4466 Fax  
Email test@test.com  
Preferred Method of Communication Email

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

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RSP Signature

Date

[Return to Home Page](#)