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POMALYST® (pomalidomide)

NDA # 204026

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

1. GOALS

The goals of the POMALYST risk evaluation and mitigation strategy are as follows:

1. To prevent the risk of embryo-fetal exposure to POMALYST.
2. To inform prescribers, patients, and pharmacists on the serious risks and safe-use conditions for POMALYST.

2. REMS ELEMENTS

2.1. Elements to Assure Safe Use

2.1.1. Healthcare providers who prescribe POMALYST are specially certified.

Celgene will ensure that healthcare providers who prescribe POMALYST are specially certified in the POMALYST REMS® program. POMALYST® (pomalidomide) is available only through a restricted distribution program, POMALYST REMS®.

To become certified, each prescriber must complete the Prescriber Enrollment Form and agree to do the following:

- a. Provide patient counseling on the benefits and risks of POMALYST therapy, including risks described in the BOXED WARNINGS.
- b. Enroll each patient by completing and submitting to the Celgene Customer Care Center via mail (86 Morris Avenue, Summit, NJ 07901), email (customercare@celgene.com), fax (1-888-432-9325), or online (www.celgeneriskmanagement.com), a signed Patient-Physician Agreement Form (PPAF) identifying the patient's risk category (see [PPAFs](#) for all six risk categories) for each new patient. In signing the PPAF, each prescriber

- acknowledges that they understand that POMALYST is available only through the POMALYST REMS[®] program, and that they must comply with program requirements.
- c. Provide contraception and emergency contraception counseling with each new prescription prior to and during POMALYST treatment.
 - d. Provide scheduled pregnancy testing for females of reproductive potential and verify negative pregnancy test results prior to writing a new prescription or subsequent prescriptions.
 - e. Report any pregnancies in female patients or female partners of male patients prescribed POMALYST immediately to Celgene Drug Safety (or Celgene Customer Care Center (1-888-423-5436)).
 - f. Complete a prescriber survey (phone or online) for every patient (new and follow-up), obtain a unique prescription authorization number for each prescription written, and include this authorization number on the prescription. The authorization number can be obtained by contacting the Celgene Customer Care Center, using the automated IVR system, or via the www.CelgeneRiskManagement.com website.
 - o For females of reproductive potential, authorization numbers are valid only for 7 days from date of last pregnancy test.
 - o Authorization numbers are valid for 30 days from the date it is issued for all other patients.
 - g. Facilitate compliance with the mandatory POMALYST REMS[®] patient survey by instructing patients to complete the mandatory surveys (phone or online) at program specified frequencies.
 - h. Prescribe no more than a 4-week (28-day) supply, with no automatic refills or telephone prescriptions.
 - i. Contact a pharmacy certified by the POMALYST REMS[®] program to fill the POMALYST prescription.
 - j. Return all unused POMALYST brought in by patients to Celgene Customer Care.
 - k. Re-enroll patients in the POMALYST REMS[®] program if POMALYST is required and previous therapy with POMALYST has been discontinued for 12 consecutive months.

Celgene will:

1. Ensure that the POMALYST REMS[®] program materials including prescriber enrollment are available on the [CelgeneRiskManagement.com](http://www.CelgeneRiskManagement.com) website or can be obtained by contacting Celgene Customer Care Center at 1-888-423-5436
2. Maintain a secure database of all POMALYST REMS[®] certified prescribers.
3. Monitor to ensure that only POMALYST REMS[®] certified prescribers are prescribing POMALYST.
4. Monitor and ensure that patients have been assigned correctly to one of the following patient risk categories. Confirm risk category when completing the PPAFs during the patient enrollment process:
 - a. **Adult female of reproductive potential:** all females who are menstruating, amenorrheic from previous medical treatments, under 50 years, and/or perimenopausal.
 - b. **Female child of reproductive potential:** all females under 18 years who are menstruating.

- c. **Adult female NOT of reproductive potential:** females who have had a natural menopause for at least 24 consecutive months, a hysterectomy, and/or bilateral oophorectomy.
 - d. **Female child NOT of reproductive potential:** all females under 18 years who are not menstruating.
 - e. **Adult males 18 years or older**
 - f. **Male child under 18 years**
5. Monitor certified prescriber compliance with the POMALYST REMS[®] program, including patient risk categorization and the appropriate corresponding counseling requirements, contraception requirements, pregnancy testing, and survey completion for all patients treated with POMALYST.
 6. Institute corrective action and prevent the certified prescriber from prescribing POMALYST if the prescriber is found to be non-compliant with the POMALYST REMS[®] program.
 7. Train POMALYST REMS[®] program certified prescribers in adverse experience reporting procedures, including the requirement to immediately report to Celgene any suspected embryo-fetal exposure to POMALYST if a pregnancy occurs.
 8. Ensure that once the prescriber submits the completed PPAF, the prescriber will receive a confirmation letter via fax or online to confirm the patient's enrollment and signify that the prescriber and patient surveys can be taken to receive an authorization number for the POMALYST prescription (for all males, the PPAF is considered the initial survey). The authorization number is written on the POMALYST prescription.
 9. Ensure that, for subsequent prescriptions, the prescriber completes a telephone or online survey designed to look for signals of at-risk behavior (e.g., pending or outdated pregnancy test), report the patient's pregnancy test results, correct assignment of risk category, and confirm or re-enforce patient understanding of contraceptive requirements. The completion of the survey will allow the prescriber to obtain a new authorization number every time a prescription for POMALYST is written.

The following materials are part of the REMS, and are appended:

- [Prescriber Enrollment Form](#)
- [Patient Prescription Form](#)
- [Patient Prescription Form \(Veterans Administration\)](#)
- [Prescriber Guide to POMALYST REMS[®] Program](#)
- [POMALYST REMS[®] At-A-Glance](#)
- [Welcome Letter](#)
- [Celgene Risk Management.com website](#)

2.1.2. POMALYST will only be dispensed by pharmacies that are specially certified.

Celgene will ensure that POMALYST is only dispensed from POMALYST REMS[®] program certified pharmacies. To become a certified pharmacy, the pharmacy must agree to do the following before filling a POMALYST prescription:

- a. Only accept prescriptions with a prescription authorization number. Authorization numbers are valid for 7 days from date of last pregnancy test for females of reproductive potential and 30 days from the date it is issued for all other patients.
- b. Dispense no more than a 4-week (28-day) supply, and require a new prescription from the patient prior to dispensing additional POMALYST.
- c. Dispense subsequent prescriptions only if there are 7 days or less remaining on an existing POMALYST prescription.
- d. Obtain a POMALYST REMS[®] confirmation number from the Celgene Customer Care Center (phone or online) and write this confirmation number on the prescription. The POMALYST REMS[®] confirmation number may be obtained using the following procedure:
 1. Enter the pharmacy identification number (NABP or DEA);
 2. Enter the prescription authorization number written on the prescription;
 3. Enter the number of capsules and milligram (mg) strength being dispensed;
 4. Dispense or ship the prescribed POMALYST within 24 hours of obtaining and recording the POMALYST REMS[®] confirmation number and confirmation date.
- e. Dispense POMALYST only after a POMALYST REMS[®] confirmation number is obtained. If no confirmation is obtained, then no POMALYST is dispensed. Contact the patient's physician and Celgene for further instruction.
- f. Accept unused POMALYST (previously dispensed) from a patient or patient caregiver and return to Celgene Corporation for proper disposal.
- g. For each patient receiving treatment, retain a record of each POMALYST prescription dispensed and the corresponding completed Education and Counseling Checklist.
- h. Complete the checklist that applies to the patient risk category written on the front of the Education and Counseling Checklist for Pharmacies.
- i. Provide counseling to patients and/or guardians of patients under 18 years of age receiving POMALYST treatment.
 - a. Counsel all patients and guardians of patients under 18 years of age on the following:
 1. The benefits and risks of POMALYST therapy.
 2. Not sharing POMALYST medication.
 3. Not donating blood while taking POMALYST, during dose interruptions, and for 4 weeks after stopping POMALYST.
 4. Not to break, chew, or open POMALYST capsules.
 5. Instructions on POMALYST dose and administration.
 6. To read the POMALYST REMS[®] program education materials and encourage compliance with the requirements.
 - b. In addition to above, counsel **Females of Reproductive Potential** on the following:
 1. The potential for embryo-fetal toxicity with exposure to POMALYST.
 2. Using 2 forms of effective birth control at the same time or abstaining from heterosexual sexual intercourse.
 3. Continuing to use 2 forms of birth control if POMALYST therapy is interrupted and for at least 4 weeks after therapy is discontinued.
 4. Obtaining a pregnancy test weekly during the first 4 weeks of POMALYST use, then a repeat pregnancy test every 4 weeks in females with regular

menstrual cycles, and every 2 weeks in females with irregular menstrual cycles.

5. The need to stop taking POMALYST and notify their POMALYST prescriber immediately if they become pregnant or suspect they may be pregnant.
- c. In addition to items listed for all patients above, counsel **Males** receiving POMALYST treatment about the potential for embryo-fetal toxicity with exposure to POMALYST and the importance of using barrier contraception by wearing a latex or synthetic condom when engaging in sexual intercourse with a female of reproductive potential even if the male receiving POMALYST has had a successful vasectomy.
 1. The need to not donate sperm while taking POMALYST, during dose interruptions, and for 4 weeks after stopping POMALYST.
- d. Counsel the **Parent or legal guardian of Female Child NOT of reproductive potential** who is receiving POMALYST treatment about the need to inform their POMALYST prescriber when the child begins menses.

Before a certified pharmacy dispenses POMALYST, Celgene will train the appropriate pharmacy staff:

1. About the POMALYST REMS[®] program
2. About the procedures for reporting adverse experiences to Celgene, including the requirement to immediately report to Celgene any suspected embryo-fetal exposure to POMALYST if a pregnancy occurs.

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

- [Pharmacy Guide to the POMALYST REMS[®] Program](#)
- [Education and Counseling Checklist for Pharmacies](#)
- [Celgene REMS Programs Pharmacy Training: the POMALYST REMS[®] Program](#)
- [Pharmacy Certification Quiz \(the POMALYST REMS[®] Program\)](#)

2.1.3. Celgene will ensure that POMALYST will only be dispensed to patients enrolled in the POMALYST REMS[®] program with evidence or other documentation of safe-use conditions.

Celgene will ensure that all patients treated with POMALYST are enrolled by a certified prescriber. The prescriber will enroll the patient by completing Patient-Physician Agreement Form and submitting the form via mail (86 Morris Avenue, Summit, NJ 07901), fax (1-888-432-9325), email (customercare@celgene.com), or online (www.celgeneriskmanagement.com) for each patient who receives POMALYST. Each patient and/or guardian of patients under 18 years of age consents to participate in the program by:

- a. acknowledging that he or she understands that:
 - i. severe birth defects or death to an unborn baby may occur if a female becomes pregnant while she is receiving POMALYST;

- ii. POMALYST must not be shared with anyone, even someone with similar symptoms;
- iii. POMALYST must be kept out of the reach of children and should NEVER be shared with females who are able to have children;
- iv. they cannot donate blood while receiving POMALYST, including dose interruptions, and for 4 weeks after stopping POMALYST;
- v. they might be asked to participate in the POMALYST Pregnancy Exposure Registry; and
- vi. they may be contacted by Celgene about following the rules of the REMS.

In addition, each patient and/or guardian of patients under 18 years of age consents to participate in the program by:

- i. agreeing to return unused POMALYST to Celgene or their POMALYST prescriber, or to the pharmacy that dispensed the POMALYST to them;
- ii. agreeing to participate in a monthly (telephone or online) survey while on POMALYST (with the exception of Adult Females Not of Reproductive Potential who are required to take a survey once every six months); and
- iii. reviewing the POMALYST REMS[®] program educational materials and asking their prescriber any questions that have not been answered.

In addition, **Females and guardians of female children** must attest to their understanding of their/their child's reproductive potential, as categorized by the prescribing physician.

Females of Reproductive Potential and guardians of Female Children of Reproductive Potential will attest that they/their child:

- a. is not currently pregnant, and will try to refrain from becoming pregnant while receiving POMALYST therapy and for at least 4 weeks after completely stopping POMALYST therapy;
- b. must not take POMALYST if pregnant, breastfeeding a baby, or not using birth control as defined in the REMS;
- c. will, unless abstinent, use contraception as defined within the REMS: for at least 4 weeks before starting POMALYST, while receiving POMALYST, during dose interruptions, and for at least 4 weeks after stopping POMALYST;
- d. will have pregnancy testing done as ordered by the certified prescriber within 10 to 14 days and 24 hours prior to starting POMALYST, every week for at least the first 4 weeks of POMALYST therapy, and then every 4 weeks if the Female of Reproductive Potential has regular menstrual cycles, or every 2 weeks if the Female of Reproductive Potential has irregular menstrual cycles, while receiving POMALYST;
- e. will immediately stop taking POMALYST and inform the certified prescriber if the patient becomes pregnant, misses a menstrual period, experiences unusual menstrual bleeding, stops using contraception, or thinks for any reason that she might be pregnant; if the prescriber is not available, the Female of Reproductive Potential or guardian of a Female Child of Reproductive Potential can call the Celgene Customer Care Center at 1-888-423-5436.

Males or guardians of Males will attest that they/their child will:

- a. never have unprotected sexual contact with a female who can become pregnant;
- b. wear a latex or synthetic condom every time the male patient has sexual contact with a female who is or who can become pregnant; continue condom use with sexual contact while the male patient is receiving POMALYST treatment, during dose interruptions, and for 4 weeks after the male patient stops taking POMALYST, even if the patient has had a successful vasectomy; and
- c. inform their certified prescriber if the male patient has unprotected sexual contact with a female who can become pregnant, or if they think for any reason that the male patient's sexual partner might be pregnant; if the prescriber is not available, the male patient or guardian of an underage male patient can call the Celgene Customer Care Center at 1-888-423-5436;
- d. not donate sperm while taking (including dose interruptions) and for 4 weeks after stopping POMALYST.

The following appended materials are part of the REMS:

- [Patient-Physician Agreement Form for Adult Males](#)
- [Patient-Physician Agreement Form for Male Child](#)
- [Patient-Physician Agreement Form for Adult Female Who Can Not Get Pregnant](#)
- [Patient-Physician Agreement Form for Adult Female Who Can Get Pregnant](#)
- [Patient-Physician Agreement Form for a Female Child Who Can Not Get Pregnant](#)
- [Patient-Physician Agreement Form for a Female Child Who Can Get Pregnant](#)
- [Patient Guide to POMALYST REMS® Program](#)
- [Emergency Contraception Brochure](#)
- [Patient Survey Reminder Card](#)
- [POMALYST Risk Evaluation and Mitigation Strategy \(REMS\) program education and prescribing safety kit](#)
- [POMALYST REMS® Patient Resource Pack Envelope](#)

2.1.4. Female patients or female partners of male patients receiving POMALYST who report a pregnancy that occurred during POMALYST therapy will be enrolled in the POMALYST Pregnancy Exposure Registry.

Upon receiving a report of pregnancy from the POMALYST REMS® program, Celgene Pregnancy Prevention Plan programs in the rest of the world, clinical trials, or directly from a prescriber, a pharmacy, or a patient, Celgene will enroll the female patient or female partner of the male patient taking POMALYST into the POMALYST Pregnancy Exposure Registry. The objectives of the registry are to monitor pregnancy outcomes in female patients of reproductive potential and male patients' female partners who are exposed to POMALYST and to understand why the POMALYST REMS® program was unsuccessful.

2.2. Implementation System

The implementation system will include the following:

- 1) Celgene will maintain a secure database of all certified entities, including enrolled patients and certified prescribers and pharmacies to monitor and evaluate implementation of the elements provided for in Sections 2.1.1, 2.1.2, and 2.1.3.
- 2) Celgene will monitor pharmacy certification compliance and address deviations by monitoring real time dispensing activity and conducting pharmacy audits.
 - a. The Celgene Customer Care Center will monitor the certified pharmacies in the manner described in the REMS supporting document to ensure only enrolled and authorized patients are receiving POMALYST. If a certified pharmacy is found to be non-compliant with the POMALYST REMS[®] program, Celgene will institute corrective action and may de-activate pharmacies for which re-training has proven ineffective, removing them from the POMALYST REMS[®] program.
 - b. Celgene will perform regular audits of contract pharmacies participating in the POMALYST REMS[®] program. For pharmacies that have been in the program for more than two years, Celgene will perform a risk-based assessment to select which pharmacies will be audited. The POMALYST REMS[®] program compliance audits will be performed by internal auditors of Celgene and/or outside auditors contracted and trained by Celgene.
- 3) Celgene will monitor and ensure that the prescriptions are filled within the allowed timeframes.
- 4) Celgene Customer Care Center will address customer complaints received that are related to the POMALYST REMS[®] program and distribution and dispensing of POMALYST.
- 5) Celgene will maintain a reporting and collection system for safety information that includes a process to monitor pregnancy testing results and pregnancy outcomes (should one occur) through the POMALYST Pregnancy Exposure Registry and to understand why the POMALYST REMS[®] program was unsuccessful for the pregnancy case in question.
- 6) Based on monitoring and evaluation of these elements to assure safe use, Celgene will take reasonable steps to work to improve implementation of these elements as applicable.
- 7) Celgene will develop and follow written procedures related to the implementation of the REMS.

2.3. Timetable for Submission of Assessment Reports

Celgene will submit REMS assessments every two years beginning with submission of the next assessment by August 3, 2016. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Celgene will submit each assessment so it will be received by the FDA on or before the due date.