CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-880

APPROVED LABELING

REVLIMID® (lenalidomide)

5 mg & 10 mg capsules

WARNINGS:

1. **POTENTIAL FOR HUMAN BIRTH DEFECTS**
2. **HEMATOLOGIC TOXICITY (NEUTROPENIA AND THROMBOCYTOPENIA)**
3. **DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLISM**

POTENTIAL FOR HUMAN BIRTH DEFECTS

WARNING: POTENTIAL FOR HUMAN BIRTH DEFECTS

LENALIDOMIDE IS AN ANALOGUE OF THALIDOMIDE. THALIDOMIDE IS A KNOWN HUMAN TERATOGEN THAT CAUSES SEVERE LIFE-THREATENING HUMAN BIRTH DEFECTS. IF LENALIDOMIDE IS TAKEN DURING PREGNANCY, IT MAY CAUSE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. FEMALES SHOULD BE ADVISED TO AVOID PREGNANCY WHILE TAKING REVLIMID® (lenalidomide).

Special Prescribing Requirements

BECAUSE OF THIS POTENTIAL TOXICITY AND TO AVOID FETAL EXPOSURE TO REVLIMID® (lenalidomide), REVLIMID® (lenalidomide) IS ONLY AVAILABLE UNDER A SPECIAL RESTRICTED DISTRIBUTION PROGRAM. THIS PROGRAM IS CALLED "REVASSIST℠". UNDER THIS PROGRAM, ONLY PRESCRIBERS AND PHARMACISTS REGISTERED WITH THE PROGRAM ARE ABLE TO PRESCRIBE AND DISPENSE THE PRODUCT. IN ADDITION, REVLIMID MUST ONLY BE DISPENSED TO PATIENTS WHO ARE REGISTERED AND MEET ALL THE CONDITIONS OF THE REVASSIST℠ PROGRAM.

PLEASE SEE THE FOLLOWING INFORMATION FOR PRESCRIBERS, FEMALE PATIENTS, AND MALE PATIENTS ABOUT THIS RESTRICTED DISTRIBUTION PROGRAM.

CELGENE'S REVASSIST℠ PROGRAM DESCRIPTION

Prescribers

REVLIMID® (lenalidomide) will be prescribed only by licensed prescribers who are registered in the RevAssist℠ program and understand the potential risk of teratogenicity if lenalidomide is used during pregnancy.

Effective contraception must be used by patients for at least 4 weeks before beginning REVLIMID® therapy, during REVLIMID® (lenalidomide) therapy, during dose interruptions and for 4 weeks following discontinuation of REVLIMID® (lenalidomide) therapy. Reliable contraception is indicated even where there has been a history of infertility, unless due to hysterectomy or because the patient has been postmenopausal naturally for at least 24 consecutive months. Two reliable forms of contraception must be used simultaneously unless continuous abstinence from heterosexual sexual contact is the chosen method. Females of childbearing potential should be referred to a qualified provider of contraceptive methods, if needed. Sexually mature females who have not undergone a hysterectomy or who have not been postmenopausal naturally for at least 24 consecutive months (i.e., who have had menses at some time in the preceding 24 consecutive months) are considered to be females of childbearing potential.

Before prescribing REVLIMID® (lenalidomide), females of childbearing potential should have 2 negative pregnancy tests (sensitivity of at least 50 mIU/mL). The first test should be performed within 10 – 14 days, and the second test within 24 hours prior to prescribing REVLIMID® (lenalidomide). A prescription for REVLIMID® (lenalidomide) for a female of childbearing potential must not be issued by the prescriber until negative pregnancy tests have been verified by the prescriber.

Male Patients: It is not known whether lenalidomide is present in the semen of patients receiving the drug. Therefore, males receiving REVLIMID® (lenalidomide) must always use a latex condom during any sexual contact with females of childbearing potential even if they have undergone a successful vasectomy.

Once treatment has started and during dose interruptions, pregnancy testing for females of childbearing potential should occur weekly during the first 4 weeks of use, then pregnancy testing should be repeated every 4 weeks in females with regular menstrual cycles. If menstrual cycles are irregular, the pregnancy testing should occur every 2 weeks. Pregnancy testing and counseling should be performed if a patient misses her period or if there is any abnormality in her pregnancy test or in her menstrual bleeding. REVLIMID® (lenalidomide) treatment must be discontinued during this evaluation.

Pregnancy test results should be verified by the prescriber and the pharmacist prior to dispensing any prescription.

If pregnancy does occur during REVLIMID® (lenalidomide) treatment, REVLIMID® (lenalidomide) must be discontinued immediately.

Any suspected fetal exposure to REVLIMID® (lenalidomide) should be reported to the FDA *via* the MedWatch number at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-4CELGEN. The patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Female Patients

REVLIMID® (lenalidomide) should be used in females of childbearing potential only when the patient MEETS ALL OF THE FOLLOWING CONDITIONS (i.e., she is unable to become pregnant while on lenalidomide therapy):

- she appears to understand the risks associated with the drug and is thought to be able to reliably carry out instructions.
- she is capable of complying with the contraceptive measures, pregnancy testing, patient registration, and patient survey as described in the RevAssist℠ program.
- she has received both oral and written warnings of the potential risks of taking lenalidomide during pregnancy and of exposing a fetus to the drug.
- she has received both oral and written warnings of the risk of possible contraception failure and of the need to use two reliable forms of contraception simultaneously, unless continuous abstinence from heterosexual sexual contact is the chosen method. Sexually mature females who have not undergone a hysterectomy or who have not been postmenopausal for at least 24 consecutive months (i.e., who have had menses at some time in the preceding 24 consecutive months) are considered to be females of childbearing potential.
- she acknowledges, in writing, her understanding of these warnings and of the need for using two reliable methods of contraception for 4 weeks prior to beginning lenalidomide therapy, during lenalidomide therapy, during dose interruptions and for 4 weeks after discontinuation of lenalidomide therapy.
- she has had two negative pregnancy tests with a sensitivity of at least 50 mIU/mL, within 10-14 days and 24 hours prior to beginning therapy.
- if the patient is between 12 and 18 years of age, her parent or legal guardian are to read the educational materials and agree to try to ensure compliance with the above.

Male Patients

REVLIMID® (lenalidomide) should be used in sexually active males when the PATIENT MEETS ALL OF THE FOLLOWING CONDITIONS:

- he appears to understand the risks associated with the drug and is thought to be able to reliably carry out instructions.
- he is capable of complying with the contraceptive measures that are appropriate for men, patient registration, and patient survey as described in the RevAssist℠ program.
- he has received both oral and written warnings of the potential risks of taking lenalidomide and exposing a fetus to the drug.

- he has received both oral and written warnings of the risk of possible contraception failure and that it is unknown whether lenalidomide is present in semen. He has been instructed that he must always use a latex condom during any sexual contact with females of childbearing potential, even if he has undergone a successful vasectomy.

- he acknowledges, in writing, his understanding of these warnings and of the need to use a latex condom during any sexual contact with females of childbearing potential, even if he has undergone a successful vasectomy. Females of childbearing potential are considered to be sexually mature females who have not undergone a hysterectomy or who have not been postmenopausal for at least 24 consecutive months (i.e., who have had menses at any time in the preceding 24 consecutive months).

- if the patient is between 12 and 18 years of age, his parent or legal guardian are to read the educational materials and agree to try to ensure compliance with the above.

HEMATOLOGIC TOXICITY (NEUTROPENIA AND THROMBOCYTOPENIA)

This drug is associated with significant neutropenia and thrombocytopenia in patients with del 5q MDS. Eighty percent of patients had to have a dose delay/reduction during the major study for the indication. Thirty-four percent of patients had to have a second dose delay/reduction. Grade 3 or 4 hematologic toxicity was seen in 80% of patients enrolled in the study. Patients on therapy should have their complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter. Patients may require dose interruption and/or reduction. Patients may require use of blood product support and/or growth factors. (SEE DOSAGE AND ADMINISTRATION)

DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLISM

This drug has demonstrated a significantly increased risk of deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients with multiple myeloma who were treated with REVLIMID® (lenalidomide) combination therapy. Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. It is not known whether prophylactic anticoagulation or antiplatelet therapy prescribed in conjunction with REVLIMID® (lenalidomide) may lessen the potential for venous thromboembolic events. The decision to take prophylactic measures should be done carefully after an assessment of an individual patient's underlying risk factors.

You can get the information about REVLIMID® and the RevAssist^{SM} program on the internet at www.REVLIMID.com or by calling the manufacturer's toll free number 1-888-4CELGEN.

DESCRIPTION

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