Pomalyst®
(pomalidomide) capsules
1 · 2 · 3 · 4 mg

The POMALYST REMS® program

Indication

POMALYST® (pomalidomide) is a thalidomide analogue indicated, in combination with dexamethasone, for adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.

Selected Important Safety Information: Boxed WARNINGS

WARNING: EMBRYO-FETAL TOXICITY and VENOUS AND ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

- **POMALYST is contraindicated in pregnancy. POMALYST is a thalidomide analogue. Thalidomide is a known human teratogen that causes severe birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.**
- **Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping POMALYST treatment.**

POMALYST is only available through a restricted distribution program called POMALYST REMS®.

Venous and Arterial Thromboembolism

- **Deep venous thrombosis (DVT), pulmonary embolism (PE), myocardial infarction, and stroke occur in patients with multiple myeloma treated with POMALYST. Prophylactic antithrombotic measures were employed in clinical trials. Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.**

CONTRAINDICATIONS

- **Pregnancy:** POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.
- **Hypersensitivity:** POMALYST is contraindicated in patients who have demonstrated severe hypersensitivity (e.g., angioedema, anaphylaxis) to pomalidomide or any of the excipients.

Please see Important Safety Information on pages 3-5 and full Prescribing Information, including Boxed WARNINGS.

Prescribing POMALYST under the POMALYST REMS® program

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FEMALES

Patient counseling Instruct your patients on why and how they and their partners should prevent pregnancy. Also inform them not to share the drug, not to donate blood, and about appropriate contraceptive use. Patients should be instructed not to extensively handle or open POMALYST capsules

Pregnancy tests only in females of reproductive potential Conduct initial pregnancy test within 10-14 days. Confirm the patient is not pregnant with a second pregnancy test within 24 hours prior to writing an initial prescription. During treatment, pregnancy testing should be repeated every 4 weeks if the patient has regular menses or is amenorrheic, or every 2 weeks if the patient has irregular menses

Enrollment Both you and your patients must understand and agree to comply with the requirements of the POMALYST REMS program, including the pregnancy-prevention steps. The POMALYST (pomalidomide) Patient-Physician Agreement Form (PPAF) must be signed by both patient and physician and faxed to the Celgene Customer Care Center at **1-888-432-9325** or be generated, signed, and submitted electronically at **www.CelgeneRiskManagement.com**. If enrolling a patient online, the system generates an online prescription that you should complete and print, sign (include the authorization number and risk category), and fax to the certified pharmacy

Complete mandatory confidential survey Your female patients will need to complete a brief survey by phone or online. You will also need to complete a mandatory survey by phone or online, after which you will receive an authorization number. You must complete this survey to obtain a new authorization number every time a POMALYST prescription is written. Female patients of reproductive potential and all female children must complete surveys monthly in order to obtain subsequent prescriptions. Adult female patients not of reproductive potential must complete surveys every 6 months

MALES

Patient counseling Instruct your patients on why and how they and their partners should prevent pregnancy. Also inform them not to share the drug, not to donate blood or sperm, and about appropriate contraceptive use. Patients should be instructed not to extensively handle or open POMALYST capsules

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Complete mandatory confidential survey Your male patients will need to complete a brief survey by phone or online. You will also need to complete a mandatory survey by phone or online, after which you will receive an authorization number. You must complete this survey to obtain a new authorization number every time a POMALYST prescription is written. The initial survey is not required for male patients, but they must complete surveys monthly in order to obtain subsequent prescriptions

ALL PATIENTS

Fax prescription Obtain an authorization number from Celgene and write it on the prescription, along with the patient risk category, and then fax it to a certified pharmacy. The certified pharmacy will contact patients for mandatory counseling and coordinate delivery of POMALYST to them.

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WARNINGS AND PRECAUTIONS

- **Embryo-Fetal Toxicity & Females of Reproductive Potential: See Boxed WARNINGS**
  - Males: Pomalidomide is present in the semen of patients receiving the drug. Males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking POMALYST and for up to 4 weeks after discontinuing POMALYST, even if they have undergone a successful vasectomy. Males must not donate sperm.
  - Blood Donation: Patients must not donate blood during treatment with POMALYST and for 4 weeks following discontinuation of POMALYST therapy because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST.
- **POMALYST REMS® Program: See Boxed WARNINGS**
  - Prescribers and pharmacies must be certified with the **POMALYST REMS** program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive POMALYST. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements.
  - Further information about the **POMALYST REMS** program is available at **www.CelgeneRiskManagement.com** or by telephone at 1-888-423-5436.

Please see additional Important Safety Information on pages 4-5 and full Prescribing Information, including Boxed WARNINGS.

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Important Safety Information (continued)

- **Venous and Arterial Thromboembolism: See Boxed WARNINGS.** Patients with known risk factors, including prior thrombosis, may be at greater risk, and actions should be taken to try to minimize all modifiable factors (e.g., hyperlipidemia, hypertension, smoking). Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.
- **Increased Mortality With Pembrolizumab:** In clinical trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- **Hematologic Toxicity:** Neutropenia (46%) was the most frequently reported Grade 3 or 4 adverse reaction in patients taking POMALYST in clinical trials, followed by anemia and thrombocytopenia. Monitor complete blood counts weekly for the first 8 weeks and monthly thereafter. Patients may require dose interruption and/or modification.
- **Hepatotoxicity:** Hepatic failure, including fatal cases, has occurred in patients treated with POMALYST. Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with POMALYST. Monitor liver function tests monthly. Stop POMALYST upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.
- **Severe Cutaneous Reactions:** Severe cutaneous reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. DRESS may present with a cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. These reactions can be fatal. Consider POMALYST interruption or discontinuation for Grade 2 or 3 skin rash. Permanently discontinue POMALYST for Grade 4 rash, exfoliative or bullous rash, or any other severe cutaneous reactions such as SJS, TEN or DRESS.
- **Dizziness and Confusional State:** In patients taking POMALYST in clinical trials, 14% experienced dizziness (1% Grade 3 or 4) and 7% a confusional state (3% Grade 3 or 4). Instruct patients to avoid situations where dizziness or confusional state may be a problem and not to take other medications that may cause dizziness or confusional state without adequate medical advice.
- **Neuropathy:** In patients taking POMALYST in clinical trials, 18% experienced neuropathy (2% Grade 3 in one trial) and 12% peripheral neuropathy.
- **Second Primary Malignancies:** Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.
- **Tumor Lysis Syndrome (TLS):** TLS may occur in patients treated with POMALYST. Patients at risk are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.
- **Hypersensitivity:** Hypersensitivity, including angioedema, anaphylaxis, and anaphylactic reactions to POMALYST have been reported. Permanently discontinue POMALYST for angioedema or anaphylaxis.

ADVERSE REACTIONS

The most common adverse reactions for POMALYST (≥30%) included fatigue and asthenia, neutropenia, anemia, constipation, nausea, diarrhea, dyspnea, upper-respiratory tract infections, back pain, and pyrexia.

In the phase III trial, nearly all patients treated with POMALYST + low-dose dex experienced at least one adverse reaction (99%). Adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥2% higher than control) included neutropenia (51%), fatigue and asthenia (47%), upper respiratory tract infection (31%), thrombocytopenia (30%), pyrexia (27%), dyspnea (25%), diarrhea (22%), constipation (22%), back pain (20%), cough (20%), pneumonia (19%), bone pain (18%), edema peripheral (17%), peripheral neuropathy (17%), muscle spasms (15%), and nausea (15%). Grade 3 or 4 adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥1% higher than control) included neutropenia (48%), thrombocytopenia (22%), and pneumonia (16%).

DRUG INTERACTIONS

Avoid concomitant use of POMALYST with strong inhibitors of CYP1A2. If concomitant use of a strong CYP1A2 inhibitor is unavoidable, reduce POMALYST dose to 2 mg.

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Important Safety Information (continued)

USE IN SPECIFIC POPULATIONS

- **Pregnancy: See Boxed WARNINGS.** If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. There is a POMALYST pregnancy exposure registry that monitors pregnancy outcomes in females exposed to POMALYST during pregnancy as well as female partners of male patients who are exposed to POMALYST. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to POMALYST to the FDA via the MedWatch program at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436.
- **Lactation:** There is no information regarding the presence of pomalidomide in human milk, the effects of POMALYST on the breastfed child, or the effects of POMALYST on milk production. Pomalidomide was excreted in the milk of lactating rats. Because many drugs are excreted in human milk and because of the potential for adverse reactions in a breastfed child from POMALYST, advise women not to breastfeed during treatment with POMALYST.
- **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.
- **Geriatric Use:** No dosage adjustment is required for POMALYST based on age. Patients >65 years of age were more likely than patients ≤65 years of age to experience pneumonia.
- **Renal Impairment:** For patients with severe renal impairment requiring dialysis, reduce the recommended dosage to 3 mg orally daily. Take dose of POMALYST following hemodialysis on hemodialysis days.
- **Hepatic Impairment:** In patients with mild to moderate hepatic impairment, reduce POMALYST dosage to 3 mg orally daily and to 2 mg orally daily in patients with severe hepatic impairment.
- **Smoking Tobacco:** Advise patients that smoking may reduce the efficacy of POMALYST. Cigarette smoking reduces pomalidomide AUC due to CYP1A2 induction.

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Bristol Myers Squibb™