

February 2013

Introducing POMALYST® (pomalidomide) capsules NOW APPROVED AND AVAILABLE in Multiple Myeloma

Dear

Celgene Corporation is pleased to announce that POMALYST (pomalidomide) capsules is now approved and available for patients with multiple myeloma who have received at least 2 prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval is based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

ICD-9 Diagnostic Codes

- The ICD-9 diagnostic codes for the approved indication of POMALYST in multiple myeloma are **203.00** and **203.02**

Dosage and Administration

- The recommended starting dose of POMALYST is 4 mg once daily orally on Days 1-21 of repeated 28-day cycles (21/28 days) until disease progression
- POMALYST may be given in combination with dexamethasone. In the study, dexamethasone was given on days 1, 8, 15, and 22, and dosed at 40 mg per day for patients 75 years or younger, or 20 mg per day for patients older than 75 years
- POMALYST may be taken with water
- Inform patients not to break, chew, or open the capsules
- POMALYST should be taken without food (at least 2 hours before or 2 hours after a meal)

WARNING: EMBRYO-FETAL TOXICITY and VENOUS 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 Thromboembolism

- **Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE) occur in patients with multiple myeloma treated with POMALYST. Prophylactic anti-thrombotic measures were employed in the clinical trial. Consider prophylactic measures after assessing an individual patient's underlying risk factors**

CONTRAINDICATIONS: Pregnancy

- POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus
- Pomalidomide is a thalidomide analogue and is teratogenic in both rats and rabbits when administered during the period of organogenesis

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Dosage Forms and Strengths

- POMALYST is available in 1 mg, 2 mg, 3 mg, and 4 mg capsules

Dose Modification Instructions for POMALYST for Hematologic Toxicities

Toxicity	Dose Modification
Neutropenia	
<ul style="list-style-type: none"> • ANC* <500 per mcL or Febrile neutropenia (fever more than or equal to 38.5°C and ANC <1,000 per mcL) • ANC return to more than or equal to 500 per mcL 	Interrupt POMALYST treatment, follow CBC weekly. Resume POMALYST at 3 mg daily.
<ul style="list-style-type: none"> • For each subsequent drop <500 per mcL • Return to more than or equal to 500 per mcL 	Interrupt POMALYST treatment. Resume POMALYST at 1 mg less than the previous dose.
Thrombocytopenia	
<ul style="list-style-type: none"> • Platelets <25,000 per mcL • Platelets return to >50,000 per mcL 	Interrupt POMALYST treatment, follow CBC weekly. Resume POMALYST treatment at 3 mg daily.
<ul style="list-style-type: none"> • For each subsequent drop <25,000 per mcL • Return to more than or equal to 50,000 per mcL 	Interrupt POMALYST treatment. Resume POMALYST at 1 mg less than previous dose.

*ANC=Absolute Neutrophil Count

- For other Grade 3 or 4 toxicities hold treatment and restart treatment at 1 mg less than the previous dose when toxicity has resolved to less than or equal to Grade 2 at the physician's discretion
- To initiate a new cycle of POMALYST, the neutrophil count must be at least 500 per mcL, the platelet count must be at least 50,000 per mcL
- If toxicities occur after dose reductions to 1 mg, then discontinue POMALYST

Important Dosing Information

- Pomalidomide may be given in combination with dexamethasone
- Pomalidomide may be taken with water
- Inform patients not to break, chew or open the capsules
- Pomalidomide should be taken without food (at least 2 hours before or 2 hours after a meal)
- Monitor CBCs every week for the first 8 weeks and monthly thereafter
- Patients may require dose interruption and/or modification
- No dosage adjustment is required for pomalidomide based on age

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Important information about POMALYST and POMALYST REMS™

- To avoid embryo-fetal exposure, POMALYST is only available under a restricted distribution program called “POMALYST REMS™”
- POMALYST is contraindicated in pregnant females and females capable of becoming pregnant. Females of reproductive potential may be treated with POMALYST provided adequate precautions are taken to avoid pregnancy
- Only prescribers and pharmacists certified by the POMALYST REMS™ program can prescribe and dispense POMALYST to patients who are enrolled and meet all the conditions of the POMALYST REMS™ program
- Information about POMALYST and the POMALYST REMS™ program can be obtained by visiting www.CelgeneRiskManagement.com, or calling the Celgene Customer Care Center toll free at 1-888-423-5436
- Effective contraception must be used by female patients of reproductive potential for at least 4 weeks before beginning POMALYST therapy, during therapy, during dose interruptions and for 4 weeks following discontinuation of POMALYST therapy
- Females of reproductive potential must 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 writing an initial prescription
- Once treatment has started and during dose interruptions, pregnancy testing for females of reproductive 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
- If pregnancy does occur during treatment, POMALYST must be discontinued immediately

Access Assistance

- Celgene Patient Support® can offer assistance with access to POMALYST for both insured and uninsured patients. This includes benefits investigations, co-pay assistance or free drug to those patients who qualify, as well as appeals support
- For assistance or more information, contact your dedicated Celgene Patient Support® Specialist at **1-800-931-8691** or visit www.CelgenePatientSupport.com

For a list of pharmacies certified in the POMALYST REMS™ program, visit www.Celgene.com/PharmacyNetwork. For more information, or if you have any questions about the recent approval of POMALYST, visit www.CelgeneRiskManagement.com or contact your local Celgene representative.

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Important Safety Information

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Embryo-Fetal Toxicity

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- **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**

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CONTRAINDICATIONS: Pregnancy

- POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus
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WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

- **Females of Reproductive Potential:** Must avoid pregnancy while taking POMALYST and for at least 4 weeks after completing therapy. Must commit either to abstain continuously from heterosexual sexual intercourse or to use 2 methods of reliable birth control, beginning 4 weeks prior to initiating treatment with POMALYST, during therapy, during dose interruptions and continuing for 4 weeks following discontinuation of POMALYST therapy. Must obtain 2 negative pregnancy tests prior to initiating therapy
- **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 28 days 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 1 month following discontinuation of the drug because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST

Important Safety Information continues on next page.

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Important Safety Information (continued)

POMALYST REMS Program

Because of the embryo-fetal risk, POMALYST is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called “**POMALYST REMS.**” Prescribers and pharmacists must be certified with the program; patients must sign an agreement form and comply with the requirements. Further information about the **POMALYST REMS** program is available at [celgeneriskmanagement.com] or by telephone at 1-888-423-5436.

Venous Thromboembolism: Patients receiving POMALYST have developed venous thromboembolic events reported as serious adverse reactions. In the trial, all patients were required to receive prophylaxis or antithrombotic treatment. The rate of DVT or PE was 3%. Consider anticoagulation prophylaxis after an assessment of each patient’s underlying risk factors.

Hematologic Toxicity: Neutropenia of any grade was reported in 50% of patients and was the most frequently reported Grade 3/4 adverse event, followed by anemia and thrombocytopenia. Monitor patients for hematologic toxicities, especially neutropenia, with complete blood counts weekly for the first 8 weeks and monthly thereafter. Treatment is continued or modified for Grade 3 or 4 hematologic toxicities based upon clinical and laboratory findings. Dosing interruptions and/or modifications are recommended to manage neutropenia and thrombocytopenia.

Hypersensitivity Reactions: Patients with a prior history of serious hypersensitivity associated with thalidomide or lenalidomide were excluded from studies and may be at higher risk of hypersensitivity.

Dizziness and Confusional State: 18% of patients experienced dizziness and 12% of patients experienced a confusional state; 1% of patients experienced grade 3/4 dizziness, and 3% of patients experienced grade 3/4 confusional state. Instruct patients to avoid situations where dizziness or confusion may be a problem and not to take other medications that may cause dizziness or confusion without adequate medical advice.

Neuropathy: 18% of patients experienced neuropathy (approximately 9% peripheral neuropathy). There were no cases of grade 3 or higher neuropathy adverse reactions reported.

Risk of Second Primary Malignancies: Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.

ADVERSE REACTIONS

In the clinical trial of 219 patients who received POMALYST alone (n=107) or POMALYST + low-dose dexamethasone (low-dose dex) (n=112), all patients had at least one treatment-emergent adverse reaction.

- In the POMALYST alone versus POMALYST + low dose dexamethasone arms, respectively, most common adverse reactions ($\geq 30\%$) included fatigue and asthenia (55%, 63%), neutropenia (52%, 47%), anemia (38%, 39%), constipation (36%, 35%), nausea (36%, 22%), diarrhea (34%, 33%), dyspnea (34%, 45%), upper respiratory tract infection (32%, 25%), back pain (32%, 30%), and pyrexia (19%, 30%)
- 90% of patients treated with POMALYST alone and 88% of patients treated with POMALYST + low-dose dex had at least one treatment-emergent NCI CTC Grade 3 or 4 adverse reaction
- In the POMALYST alone versus POMALYST + low dose dexamethasone arms, respectively, most common Grade 3/4 adverse reactions ($\geq 15\%$) included neutropenia (47%, 38%), anemia (22%, 21%), thrombocytopenia (22%, 19%), and pneumonia (16%, 23%). For other Grade 3 or 4 toxicities besides neutropenia and thrombocytopenia, hold treatment and restart treatment at 1 mg less than the previous dose when toxicity has resolved to less than or equal to Grade 2 at the physician’s discretion
- 67% of patients treated with POMALYST and 62% of patients treated with POMALYST + low-dose dex had at least one treatment-emergent serious adverse reaction
- In the POMALYST alone versus POMALYST + low dose dexamethasone arms, respectively, most common serious adverse reactions ($\geq 5\%$) were pneumonia (14%, 19%), renal failure (8%, 6%), dyspnea (5%, 6%), sepsis (6%, 3%), pyrexia (3%, 5%), dehydration (5%, 3%), hypercalcemia (5%, 2%), urinary tract infection (0%, 5%), and febrile neutropenia (5%, 1%)

Important Safety Information continues on next page.

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Important Safety Information (continued)

DRUG INTERACTIONS

No formal drug interaction studies have been conducted with POMALYST. Pomalidomide is primarily metabolized by CYP1A2 and CYP3A. Pomalidomide is also a substrate for P-glycoprotein (P-gp). Coadministration of POMALYST with drugs that are strong inhibitors or inducers of CYP1A2, CYP3A, or P-gp should be avoided. Cigarette smoking may reduce pomalidomide exposure due to CYP1A2 induction. Patients should be advised that smoking may reduce the efficacy of pomalidomide.

USE IN SPECIFIC POPULATIONS

Pregnancy: 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. Report any suspected fetal exposure to POMALYST to the FDA via the MedWatch program at 1-800-332-1088 and also to Celgene Corporation at 1-888-423-5436.

Nursing Mothers: It is not known if pomalidomide is excreted in human milk. 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 nursing infants from POMALYST, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness of POMALYST in patients under the age of 18 have not been established.

Geriatric Use: No dosage adjustment is required for POMALYST based on age. Patients greater than or equal to 65 years of age were more likely than patients less than or equal to 65 years of age to experience pneumonia.

Renal and Hepatic Impairment: Pomalidomide is metabolized in the liver. Pomalidomide and its metabolites are primarily excreted by the kidneys. The influence of renal and hepatic impairment on the safety, efficacy, and pharmacokinetics of pomalidomide has not been evaluated. Avoid POMALYST in patients with a serum creatinine >3.0 mg/dL. Avoid POMALYST in patients with serum bilirubin >2.0 mg/dL and AST/ALT >3.0 x ULN.

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Sincerely,



Gordon Willcox
Senior Director, National and Regional Accounts
US Hematology & Oncology
Celgene Corporation



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