**POMALYST®** (pomalidomide) capsule is an oral immunomodulatory therapy (a thalidomide analogue) indicated for patients with multiple myeloma (MM) who have received at least two prior therapies including REVLIMID® (lenalidomide) and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy.

POMALYST was approved for this indication by the U.S. Food and Drug Administration (FDA) on February 10, 2013.

POMALYST may be given in combination with dexamethasone (dex), a commonly used treatment for patients with MM, at the discretion of the physician. It is also being studied for the treatment of myelofibrosis and other serious diseases with high unmet needs for patients.

**How does POMALYST work?**

POMALYST is an IMiDs® compound. IMiDs compounds are small molecule, orally available therapies that modulate the immune system and other biological targets through multiple mechanisms of action, not all of which have been fully characterized.

POMALYST is an analogue of thalidomide, a modulator of the immune system that has anti-tumor activity. POMALYST has significant activity against myeloma cells, including those that are no longer responsive to other therapies. In cell cultures, POMALYST was shown to inhibit tumor cell growth and trigger tumor cell death. POMALYST also enhances the body’s immune response to the tumor, specifically through T cells and natural killer (NK) cells and by reducing production of pro-inflammatory molecules made by the immune system.
What has the clinical data for POMALYST shown for patients with MM?

POMALYST is active and generally well tolerated in heavily pretreated MM patients. Clinical trials of POMALYST in MM included patients who were refractory (did not respond to treatment) and those who achieved an initial response but then relapsed. These patients with relapsed or refractory MM (RRMM) received at least two prior therapies (including lenalidomide and bortezomib) and experienced disease progression within 60 days of their last treatment.

In a phase II clinical trial (MM-002) of 221 patients with RRMM, patients treated with POMALYST and low-dose dex (N=113) had an overall response rate of 29.2% compared with 7.4% for those treated with POMALYST alone (N=108). Partial response rates in the analysis were 28.3% for patients treated with the combination of POMALYST and low-dose dex versus 7.4% for those treated with POMALYST alone.

The most common adverse reactions (≥30%) included fatigue and asthenia (lack of strength or energy), neutropenia (low white blood cell count), anemia (low red blood cell count), constipation, nausea, diarrhea, dyspnea (shortness of breath), back pain and pyrexia (fever).

• MM-002 was the pivotal trial evaluated by the FDA for approval of POMALYST for the treatment of patients with MM who experienced disease progression on or within 60 days of their last treatment. POMALYST approval is based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

A recent phase III clinical trial (MM-003) demonstrated significantly improved median progression-free survival of 15.7 weeks for patients with RRMM who were treated with POMALYST plus low-dose dex compared with 8.0 weeks for those treated with high-dose dex. Median overall survival was also significantly improved for the POMALYST plus low-dose dex arm compared with high-dose dex (median not reached vs. 34 weeks, respectively).• Findings from this trial will be used to support the Marketing Authorization Application that was submitted to the European Medicines Agency (EMA) in May 2012.

A phase III clinical trial evaluating pomalidomide in combination with bortezomib and dex vs. bortezomib and dex alone in subjects with RRMM is expected to commence in early 2013.
Important Safety Information

**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.

**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.

**POMALYST REMS Program**

Because of the embryo-fetal risk, POMALYST is available only through a restricted distribution 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](http://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 (≥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 (≥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 (≥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%)

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.

Please see full Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.