PDL NEW DRUG REVIEW

Proprietary Name: Pomalyst®
Common Name: pomalidomide
PDL Category: Antineoplastics Immunomodulators

Comparable Products	Preferred Drug List Status
Doxorubicin	Recommended
Revlimid	Non-Recommended
Thalomid	Preferred
Velcade	Recommended

Summary

Indications and Usage: For those 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. Clinical benefit, such as improvement in survival or symptoms, has not been verified. This is a pregnancy category X medication. The safety and efficacy of use in children under the age of 18 have not been established.

Drug Interactions: Formal drug interactions have not been performed with Pomalyst®; however, it is known that pomalidomide is primarily metabolized by CYP1A12 and CYP3A4, as well as being a substrate for P-glycoprotein (P-gp). Thus, it is recommended that concomitant use of Pomalyst® with strong inhibitors of CYP1A2, CYP3A4, or P-gp be avoided, due to the potential of increased exposure of Pomalyst®. Furthermore, it is recommended that the concomitant use of Pomalyst® with strong inducers of CYP1A2, CYP3A4, or P-gp be avoided, due to a decrease in exposure.

Cigarette smoking may reduce the efficacy of pomalidomide due to CYP1A2 induction. Patients should be advised of the potential for decreased efficacy.

Dosage Forms: Capsules: 1mg, 2mg, 3mg, and 4mg

Recommended Dosage: Taken as 4mg once daily on days 1-21 of repeated 28-day cycles until disease progression. It may be given in combination with dexamethasone. It may be taken with water but should be taken without food (at least 2 hours before or 2 hours after a meal).

Prior to starting Pomalyst® therapy, females of reproductive potential must have two negative pregnancy tests, and use of 2 forms of contraception must be implemented during treatment.

As neutropenia of any grade was reported in 50% of those taking Pomalyst® during clinical trials, it is recommended that all be monitored for hematologic toxicities, especially neutropenia. Complete blood counts should be monitored weekly for the first 8 weeks of treatment, and then monthly thereafter. Dependent upon results of lab tests, dose interruption and/or dose modification may be required. Please refer to the prescribing information for specific dose modifications in those with hematologic toxicities.

It is recommended to avoid Pomalyst® use in those with a serum creatinine greater than 3.0mg/dl, as this population was excluded from clinical trials. Additionally, it is recommended to avoid Pomalyst® use in those with serum bilirubin greater than 2.0mg/dl and AST/ALT greater than 3 times the upper normal limit (UNL), as this population was excluded from clinical trials.

Common Adverse Drug Reactions: *There was no placebo data available.* Some of the most common adverse events reported with Pomalyst®/Pomalyst® plus low dose dexamethasone includes fatigue/asthenia (55/63%), pyrexia (19/30%),

peripheral edema (23/16%), chills (9/11%), neutropenia (52/47%), anemia (38/39%), thrombocytopenia (25/23%), leukopenia (11/18%), lymphopenia (4/15%), constipation (36/35%), diarrhea (34/33%), nausea (36/22%), vomiting (14/13%), pneumonia (23/29%), upper respiratory tract infection (32/25%), urinary tract infection (8/16%), back pain (32/30%), musculoskeletal chest pain (22/20%), muscle spasms (19/19%), arthralgia (16/15%), dyspnea (34/45%), cough (14/21%), epistaxis (15/11%), renal failure (15/10%), decreased appetite (22/18%), rash (22/16%), pruritus (15/11%), dizziness (20/17%), tremor (9/13%), headache (13/8%), insomnia (7/14%), and confusional state (10/13%).

Contraindications: In females who are pregnant.

Manufacturer: Celgene Corporation

Analysis: Pomalidomide, the active ingredient of Pomalyst®, is an analogue of thalidomide and an immunomodulatory antineoplastic agent. It was found *in vitro* to inhibit proliferation and induce apoptosis of hematopoietic tumor cells. Also, pomalidomide inhibited the proliferation of lenalidomide-resistant multiple myeloma cell lines and synergized with dexamethasone in both lenalidomide-sensitive and lenalidomide-resistant cell lines to induce tumor cell apoptosis. Pomalidomide enhanced T cell- and natural killer (NK) cell-mediated immunity and inhibited production of pro-inflammatory cytokines.

Pomalidomide (Pomalyst®) carries a box warning regarding the risk of embryo-fetal toxicity with use, and thus is contraindicated in pregnancy. It is required that two negative pregnancy tests be obtained prior to starting Pomalyst® treatment. Furthermore, two forms of contraception must be used by females of reproductive potential, or they must continuously abstain from heterosexual sex during and for 4 weeks after stopping treatment. As such, Pomalyst® is only available thought the restricted distribution program. A boxed warning for venous thromboembolism also exists with Pomalyst®. DVT and PE may occur in those being treated for multiple myeloma. It is thus recommended that prophylactic measures be considered after assessing for each patient's underlying risk factors.

Due to the embryo-fetal risk associated with Pomalyst®, it is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS), called the 'Pomalyst REMS'. There are several criteria for this program, and they include that the prescribers must be certified with the Pomalyst REMS program, the patients must sign a patient-prescriber agreement form and comply with the REMS requirements (this includes but is not limited to that female patients of reproductive potential who are not pregnant must comply with pregnancy testing and contraception requirement, and pharmacies must be certified with the program and dispense only to those who are certified to receive the medication).

The efficacy of pomalidomide was established in a Phase 2, multicenter, randomized, open-label study that included adults (N=221) with relapsed multiple myeloma who were refractory to the last myeloma treatment and had received lenalidomide and bortezomib. Patients were randomized to receive Pomalyst® monotherapy or Pomalyst® with low dose dexamethasone, but those in monotherapy group were allowed to add low dose dexamethasone upon disease progression. The overall response rate (ORR) and duration of response (DOR) were assessed. Results suggested that the ORR with Pomalyst® was 7.4% and with Pomalyst® plus dexamethasone (combo group) was 29.2%. The complete response was 7.4% and 28.3%, respectively. The DOR was not established (the median has not yet been reached) in the monotherapy group but was 7.4 months for the combo group.

It is recommended that Pomalyst® be added to the Recommended Drug List as a non-recommended drug, as it is not intended as a first-line treatment option.

PDL Placement: ☐ **Recommended**
☒ **Non-Recommended**

References

[1] Pomalyst [package insert]. Summit, NJ: Celgene Corporation; 2013.