# PDL DRUG REVIEW

**Proprietary Name: Xpovio®**
**Common Name: selinoexor**
**PDL Category: Antineoplastics**

## Summary


**Pharmacology/Usage:** Selinexor, the active ingredient of Xpovio®, is an orally available nuclear export inhibitor. In nonclinical studies, selinexor reversibly inhibits nuclear export of tumor suppressor proteins (TSPs), growth regulators, and mRNAs of oncogenic proteins by blocking exportin 1 (XPO1). XPO1 inhibition by selinexor leads to accumulation of TSPs in the nucleus, reductions in several oncoproteins (such as c-myc and cyclin D1), cell cycle arrest, and apoptosis of cancer cells.

**Indication:** In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least 4 prior therapies and whose disease is refractory to at least 2 proteasome inhibitors, at least 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

There is no pregnancy category for this medication; however, the risk summary indicates that based on findings in animal studies and its mechanism of action, Xpovio® can cause fetal harm when given to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. Advise pregnant women of the risks to a fetus. Prior to starting treatment, verify the pregnancy status of females of reproductive potential and use effective contraception during treatment and for 1 week after the last dose. The safety and efficacy of use in the pediatric population have not been established.

**Dosage Forms:** Film-Coated Tablets: 20mg. Do not break, chew, crush, or divide the tablets.

**Recommended Dosage:** The recommended dosage is 80mg PO on days 1 and 3 of each week until disease progression or unacceptable toxicity. The recommended starting dosage of dexamethasone is 20mg PO with each dose of Xpovio® on days 1 and 3 of each week.

Monitor complete blood counts (CBCs), standard blood chemistry, and body weight at baseline and during treatment as clinically indicated. Monitor more frequently during the first 2 months of treatment.

Advise patients to maintain adequate fluid and caloric intake throughout treatment. Consider IV hydration for patients at risk of dehydration. Provide prophylactic concomitant treatment with a 5-HT3 antagonist and/or other anti-nausea agents prior to and during treatment with Xpovio®.

Recommended dosage reductions and dosage modifications for adverse reactions, such as hematologic and non-hematologic adverse reactions, can be found in the prescribing information. Hematologic adverse reactions may

include thrombocytopenia, neutropenia, and anemia. Non-hematologic adverse reactions may include hyponatremia, fatigue, nausea/vomiting, diarrhea, weight loss and anorexia. Dose adjustments are not required with renal impairment or mild hepatic impairment. The effect of moderate and severe hepatic impairment on selinexor pharmacokinetics is unknown.

**Drug Interactions:** There are no drug interactions listed with this product.

**Common Adverse Drug Reactions:** *Listed % incidence for adverse drug reactions= reported % incidence for drug (Xpovio® plus dexamethasone) for any grade. There was no comparator information found in the prescribing information.* The reported adverse events included thrombocytopenia (74%), fatigue (73%), nausea (72%), anemia (59%), decreased appetite (53%), weight decreased (47%), diarrhea (44%), vomiting (41%), hyponatremia (39%), neutropenia (34%), leukopenia (28%), constipation (25%), dyspnea (24%), upper respiratory tract infection (21%), cough (16%), mental status change (16%), pyrexia (16%), hyperglycemia (15%), dizziness (15%), insomnia (15%), lymphopenia (15%), dehydration (14%), hypercreatininemia (14%), pneumonia (13%), epistaxis (12%), hypokalemia (12%), dysgeusia (11%), vision blurred (10%), and headache (10%).

Xpovio® can cause thrombocytopenia, leading to potentially fatal hemorrhage. The median time to onset of the first event was 22 days. Monitor platelet counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first 2 months of treatment.

Xpovio® can cause neutropenia, potentially increasing the risk of infection. The median time to onset of the first event was 25 days. Febrile neutropenia was reported in 3% of patients. Obtain neutrophil counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first 2 months of treatment. Consider supportive measures including antimicrobials for signs of infection and use of growth factors.

Nausea/vomiting and diarrhea were reported with Xpovio® use. The median time to onset of the first nausea event was 3 days, the median time to onset of the first vomiting event was 5 days, and the median time to onset of diarrhea was 15 days. Provide prophylactic 5-HT3 antagonists and/or other anti-nausea medications prior to and during treatment with Xpovio®. Manage diarrhea by dose modifications and/or standard anti-diarrheal agents.

Xpovio® can cause hyponatremia. The median time to onset of the first event was 8 days. Monitor sodium level at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first 2 months of treatment. Correct sodium levels for concurrent hyperglycemia and high serum paraprotein levels.

In patients receiving Xpovio®, 52% experienced any grade of infection. The median time to onset was 54 days for pneumonia and 42 days for sepsis.

Neurological toxicities also occurred in patients treated with Xpovio®. Neurological adverse reactions including dizziness, syncope, depressed levels of consciousness, and mental status changes occurred in 30% of patients. The median time to the first event was 15 days. Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status change.

**Contraindications:** There are no contraindications listed with this product.

**Manufacturer:** Karyopharm Therapeutics, Inc

**Analysis:** The efficacy of Xpovio® in combination with dexamethasone was assessed in a multicenter, single-arm, open-label study (STORM) that included patients with RRMM. STORM part 2 included RRMM patients (N=122) who had previously received ≥3 anti-myeloma treatment regimens, including an alkylating agent, glucocorticoids, bortezomib, carfilzomib, lenalidomide, pomalidomide, and an anti-CD38 monoclonal antibody. In addition, myeloma was documented to be refractory to glucocorticoids, a proteasome inhibitor, an immunomodulatory agent, an anti-CD38 monoclonal antibody, and to the last line of therapy.

In STORM part 2, of the 122 patients treated with Xpovio® 80mg plus dexamethasone, 83 patients had RRMM that was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab. Treatment continued until disease progression, death, or unacceptable toxicity. The median age of these 83 adults was 65 years, while 61% were male and 70% were white. The median years from diagnosis to start of study treatment was 7 years.

The major efficacy outcome measure was overall response rate (ORR), as assessed by an Independent Review Committee (IRC) based on the International Myeloma Working Group (IMWG) Uniform Response Criteria for multiple myeloma. The approval of Xpovio® was based upon the safety and efficacy in a prespecified subgroup analysis of the 83 patients whose disease was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab, as the benefit-risk ratio appeared to be greater in this more heavily pre-treated population than in the overall trial population. Overall response rates can be found in the table below, which was adapted from the prescribing information. The median time to first response was 4 weeks (range 1 to 10 weeks), and the median duration of response was 3.8 months.

| Response | Xpovio® plus dexamethasone (N=83) |
|---|---|
| Overall Response Rate | 21 (25.3%) |
| Stringent Complete Response | 1 (1%) |
| Complete Response | 0 |
| Very Good Partial Response | 4 (5%) |
| Partial Response | 16 (19%) |

**Place in Therapy:** Xpovio® is an oral nuclear export inhibitor indicated in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least 4 prior therapies and whose disease is refractory to at least 2 proteasome inhibitors, at least 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. In a single study with a pre-specified subgroup analysis of 83 patients, the overall response rate was 25%.

It is recommended that Xpovio® should be Non-Recommended with Conditions in order to confirm the appropriate diagnosis and clinical parameters for use.

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

## References

[1] Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics; 2019.


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