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for an interactive clinical discussion on XPOVIO® (selinexor)

Karyopharm Therapeutics

XPOVIO (selinexor) with Bortezomib and Dexamethasone (XVd): A Treatment Option for Multiple Myeloma as Early as First Relapse

PRESENTED BY: Rajesh Behl, MD

Alta Bates Summit Comprehensive Cancer Center

DATE AND TIME: Wednesday, July 17, 2024, 6:30 PM Pacific

LOCATION: Fleming's Prime Steakhouse and Wine Bar

180 El Camino Real G-2

Palo Alto, California 94304

RSVP:

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KAR0003538 *Please reference this number during registration.*

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INDICATIONS

XPOVIO® (selinexor) is a prescription medicine approved:

- in combination with bortezomib and dexamethasone (XVd) to treat adult patients with multiple myeloma (MM) who have received at least one prior therapy.
- in combination with dexamethasone (Xd) for the treatment of adult patients with relapsed or refractory multiple myeloma (MM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.
- for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.
  - 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 confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma (MM) and developed or worsened in patients with DLBCL.

Thrombocytopenia is the leading cause of dosage modifications. Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Monitor patients for signs and symptoms of bleeding. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Neutropenia: XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection. Monitor more frequently during the first 3 months of treatment. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients with MM and DLBCL.

Nausea/Vomiting/Diarrhea: Provide prophylactic antiemetics as needed.

Anorexia/Weight Loss: Monitor weight, nutritional status, and volume status at baseline and throughout treatment and provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

Hyponatremia: XPOVIO can cause severe or life-threatening hyponatremia.

Monitor sodium level at baseline and throughout treatment.

Serious Infection: XPOVIO can cause serious and fatal infections. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Neurological Toxicity: XPOVIO can cause life-threatening neurological toxicities.

Coadministration of XPOVIO with other products that cause dizziness or mental status changes may increase the risk of neurological toxicity.

Advise patients to refrain from driving and engaging in hazardous occupations or activities, until the neurological toxicity fully resolves. Institute fall precautions as appropriate.

Embryo-Fetal Toxicity: XPOVIO can cause fetal harm when administered to a pregnant woman.

Advise pregnant women of the potential risk to a fetus.

Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

Cataracts: New onset or exacerbation of cataract has occurred during treatment with XPOVIO. In patients with MM who received XPOVIO 100mg once weekly, the incidence of new onset or worsening cataract requiring clinical intervention was reported.

ADVERSE REACTIONS

MM: The most common adverse reactions (ARs) (≥20%) in patients with multiple myeloma who received XVd were fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract, and vomiting.

In patients with MM, who received XVd, fatal ARs occurred in 6% of patients within 30 days of last treatment. Serious ARs occurred in 52% of patients.

Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, peripheral neuropathy and vomiting. Adverse reactions led to XPOVIO dose interruption in 83% of patients and dose reduction in 64% of patients.

The most common ARs in ≥20% of patients with MM who received Xd were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

In patients with MM, who received Xd fatal ARs occurred in 9% of patients. Serious ARs occurred in 58% of patients.

Treatment discontinuation rate due to ARs was 27%. The most frequent ARs requiring permanent discontinuation in ≥4% of patients included fatigue, nausea, and thrombocytopenia. In patients with MM, adverse reactions led to XPOVIO dose interruption in 65% of patients and dose reduction in 53%.

DLBCL: The most common ARs, excluding laboratory abnormalities, in ≥20% of patients with DLBCL were fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities in ≥15% of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in ≥5% were thrombocytopenia, lymphopenia, and neutropenia.

In patients with DLBCL, fatal ARs occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal AR was infection (4.5% of patients). Serious ARs occurred in 46% of patients; the most frequent serious AR was infection.

Discontinuation due to ARs occurred in 17% of patients. In patients with DLBCL, adverse reactions led to XPOVIO dose interruption in 61% of patients and dose reduction in 49%, with 17% of all patients having 2 or more dose reductions.

USE IN SPECIFIC POPULATIONS

In MM, no overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥75 years old, with MM who received Xd, had a higher incidence of discontinuation due to an AR than younger patients, a higher incidence of serious ARs, and a higher incidence of fatal ARs.

The effect of end-stage renal disease (CL_{CR} <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

Please see full Prescribing Information.

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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