NEW INDICATION

XPOVIO® (selinexor)

Dear healthcare professional,
We're excited to announce that XPOVIO is **NOW APPROVED** as early as 1st relapse for your patients with multiple myeloma (MM).

BOSTON Trial: Phase 3, global, randomized, open-label study of patients with MM who have received 1-3 prior therapies that compared the XPOVIO + Vd regimen to Vd[1]

N=402
Patients with MM who have received 1-3 prior therapies were randomized into 2 study arms

- XVd (n=195): Once-weekly selinexor + bortezomib with twice-weekly dexamethasone
- Vd (n=207): Twice-weekly bortezomib + four times weekly dexamethasone

Primary endpoint:
Progression-free survival (PFS)

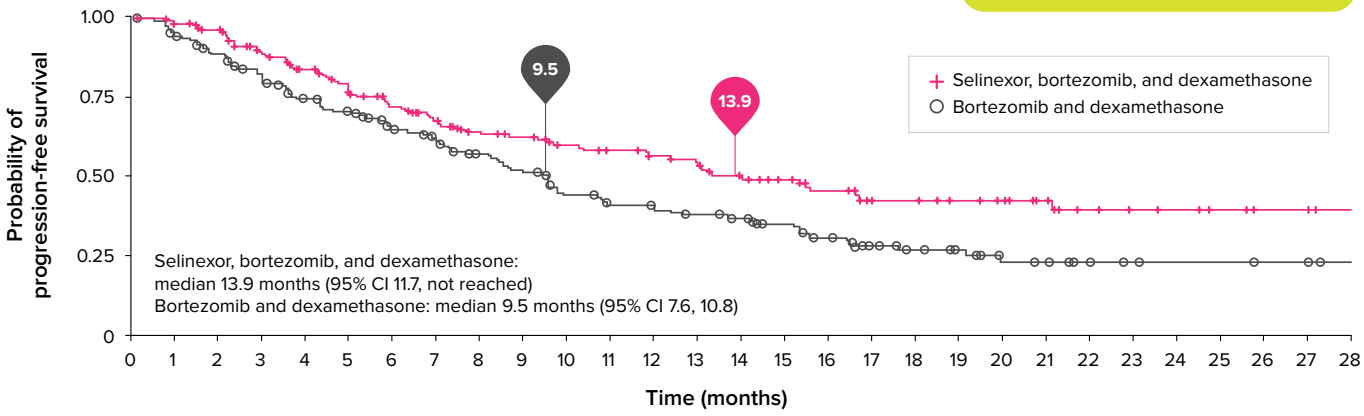
Select secondary endpoints:
Overall response rate (ORR) and ≥very good partial response (VGPR) rate

The BOSTON trial evaluated real-world patients with a broad range of characteristics, nearly half of which had high-risk cytogenetics.[1]

Once-weekly, oral XPOVIO + Vd delivered an early and sustained PFS advantage versus twice-weekly Vd[1]

30% reduction in risk of progression or death[1]
Hazard ratio: 0.70 (95% CI 0.53-0.93), *p*=0.0075

Kaplan-Meier Curve for progression-free survival (PFS)[1a]



Hazard ratio (HR) is based on stratified Cox's proportional hazard regression modeling, *p*-value based on stratified log-rank test.

[a]According to the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma, as assessed by an Independent Review Committee (IRC).
XVd=XPOVIO® (selinexor) with Velcade® (bortezomib) and dexamethasone; Vd=Velcade and dexamethasone.

INDICATION

XPOVIO® (selinexor) is a prescription medicine approved:

- in combination with bortezomib and dexamethasone (XVd) to treat adult patients with multiple myeloma who have received at least one prior therapy.

IMPORTANT SAFETY INFORMATION

- XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma.

Please see Important Safety Information throughout and full Prescribing Information.

XPOVIO® (selinexor)

Responses observed with oral, once-weekly XPOVIO + Vd were rapid and durable versus twice-weekly Vd[1]

Median time to response[1]

1.4 months once-weekly XPOVIO + Vd vs **1.6 months** twice-weekly Vd

Median duration of response[1]

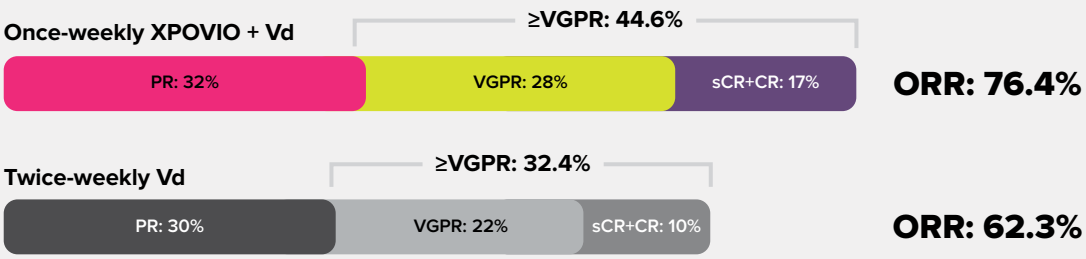
20.3 months once-weekly XPOVIO + Vd vs **12.9 months** twice-weekly Vd

Among patients who received XPOVIO, the median duration of XPOVIO treatment was 29 weeks (range: 1 to 120 weeks), and the median dose was 80 mg (range: 30 to 137 mg) per week.[1]

Depth of response observed with once-weekly XPOVIO + Vd was significant versus twice-weekly Vd (p=0.0082)[1]

Improvement in ORR was observed across a variety of patient subgroups[1]

Overall response rates (ORR) demonstrated in the BOSTON trial[1]:



CR=complete response; PR=partial response; sCR=stringent complete response; VGPR=very good partial response.

XPOVIO + Vd offers a well-established safety profile that is generally manageable and/or reversible with appropriate prophylactic measures and supportive care[2]

- 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[1]
- 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[1]
- Fatal adverse reactions occurred in 6% of patients within 30 days of last treatment, including pneumonia (n=3) and sepsis (n=3)[1]

IMPORTANT SAFETY INFORMATION (cont'd)

- 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.
- 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.

Please see Important Safety Information throughout and full Prescribing Information.

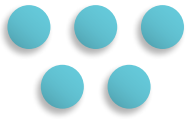
XPOVIO® (selinexor)

How to take oral, once-weekly XPOVIO + Vd[1]

The recommended dosage of **XPOVIO is 100 mg** taken orally once weekly on day 1 of each week until disease progression or unacceptable toxicity in combination with[1]:

- Bortezomib 1.3 mg/m^2 administered subcutaneously once weekly on day 1 of each week for 4 weeks followed by 1 week off
- Dexamethasone 20 mg taken orally twice weekly on days 1 and 2 of each week

For additional information regarding the dosing and administration of bortezomib or dexamethasone, refer to the prescribing information for each.



20 mg x 5

Adverse reactions may be resolved with dose modifications and/or supportive care[1]

KaryForward is a patient support program by Karyopharm Therapeutics dedicated to providing assistance and resources to patients and their caregivers for XPOVIO treatment

KaryFORWARD® PATIENT SUPPORT BY KARYOPHARM

ENROLL YOUR PATIENTS OR LEARN MORE

CALL: 1-877-KARY4WD (1-877-527-9493)
Monday through Friday, 8 am to 8 pm ET

VISIT: KaryForward.com

IMPORTANT SAFETY INFORMATION (cont'd)

- XPOVIO can cause severe gastrointestinal toxicities in patients.
- Provide prophylactic antiemetics or treatment as needed.
- Monitor weight, nutritional status, and volume status at baseline and throughout treatment and provide nutritional support, fluids, and electrolyte repletion as clinically indicated.
- XPOVIO can cause severe or life-threatening hyponatremia.
- Monitor sodium level at baseline and throughout treatment.
- XPOVIO can cause serious and fatal infections. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.
- 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.

Please see Important Safety Information throughout and full Prescribing Information.

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Contact a Karyopharm Representative to learn more about XPOVIO and how to access treatment for your patients.

IMPORTANT SAFETY INFORMATION (cont'd)

- 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.
- New onset or exacerbation of cataract has occurred during treatment with XPOVIO. The incidence of new onset or worsening cataract requiring clinical intervention was reported.

ADVERSE REACTIONS

- 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.
- Grade 3-4 laboratory abnormalities (≥10%) were thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia.
- 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.

USE IN SPECIFIC POPULATIONS

- No overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥65 years old had a higher incidence of discontinuation due to an adverse reaction (AR) and a higher incidence of serious ARs than younger patients. 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.

References: 1. XPOVIO (selinexor) [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; December 2020.
2. Data on File.

Karyopharm® Therapeutics