XPOVIO® (selinexor)

Multiple Myeloma

Getting Patients Started Guide

For patients who have relapsed, XPOVIO® provides an opportunity to introduce a different drug class to treat their disease. Being familiar with some key considerations can be helpful when starting and managing patients on XPOVIO, especially in their first month of treatment.

Key considerations when starting a patient on XPOVIO:

1. **Set expectations**
   Empower patients by educating them on what to expect
2. **Proactively manage nausea**
   Administer two antiemetic medications prior to and during treatment
3. **Assess for dose modifications**
   Monitor for the need for dose modifications to manage potential adverse reactions
4. **Connect patients with additional support**
   Enroll patients in the KaryForward® patient support program and provide support resources

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

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

Please see Important Safety Information throughout this brochure, and accompanying full Prescribing Information.

1 Set expectations

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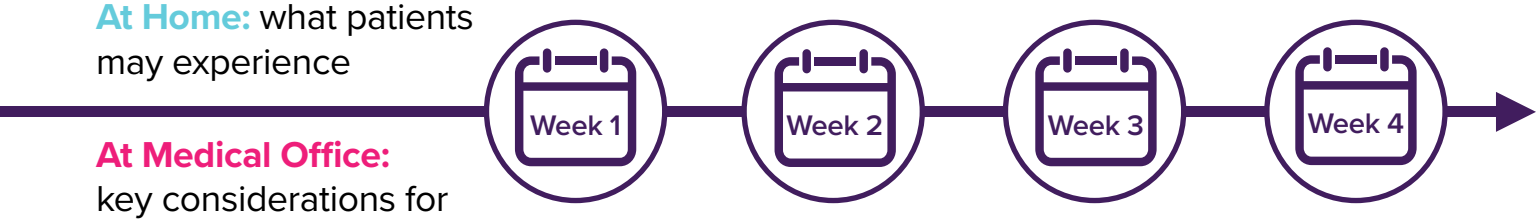
Considerations when starting a patient on XPOVIO[1–5]

Ensure patients stay hydrated, well-nourished, and maintain their energy levels

Fatigue

Nausea

At Home: what patients may experience



At Medical Office: key considerations for the healthcare team

Median time to onset

Nausea	Hyponatremia	Thrombocytopenia
First week	Within 3 weeks	Within 3–4 weeks

Monitor patients (e.g., labs, weight, nutritional status) and assess need for dose modification to mitigate adverse reactions (ARs)

Monitor more frequently during the first **3 months**

IMPORTANT SAFETY INFORMATION (cont'd)

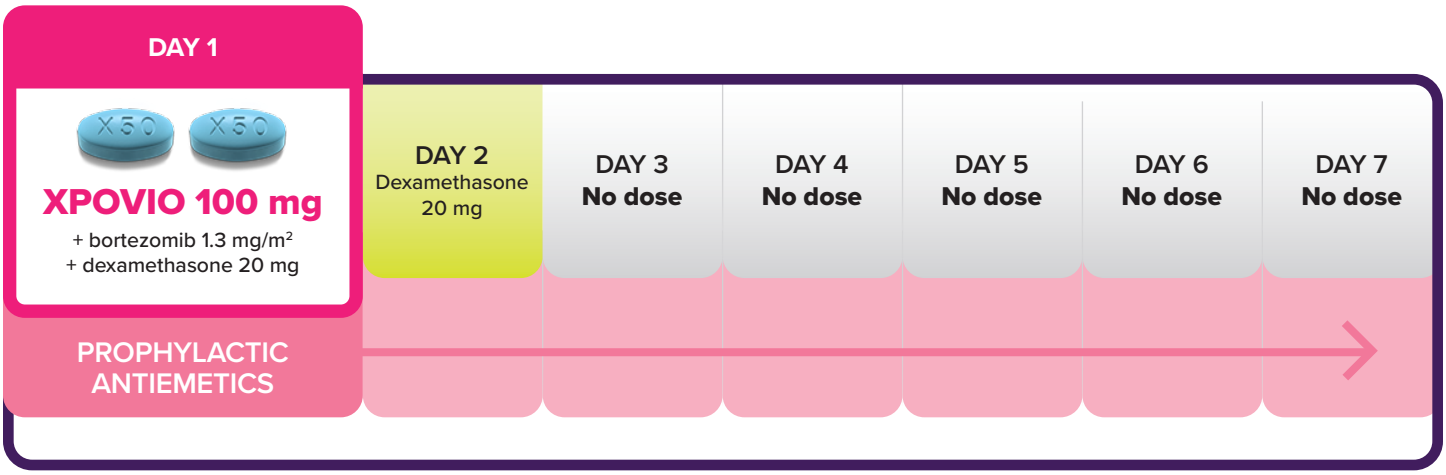
Neutropenia: XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection. Monitor more frequently during the first 3 months of treatment. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue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

Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients.

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

Please see Important Safety Information throughout this brochure, and accompanying full Prescribing Information.

Recommended administration schedule[1]



XPOVIO 100 mg taken orally once weekly on Day 1 of each week until disease progression or unacceptable toxicity in combination with:

- **Bortezomib 1.3 mg/m² 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 and dexamethasone, refer to the prescribing information for each

IMPORTANT SAFETY INFORMATION (cont'd)

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 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.

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2 Proactively manage nausea

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Before starting therapy and during treatment with XPOVIO, provide 2 antiemetics[1,5]

5-HT3 antagonist[1]

e.g., Ondansetron[8]

8 mg taken orally 30 to 60 minutes prior to each dose of XPOVIO and scheduled for every 8 hours for 2 days following dosing[7,8]

+

D2 & 5-HT2A antagonist[5–7,9]

e.g., Olanzapine

2.5 mg–5.0 mg taken orally at night[7]

NK-1 antagonists (e.g., aprepritant or rolapitant[10,11]) can be used in place of a D2/5-HT2A antagonist.[5,6]

Antiemetics such as NK-1 inhibitors and olanzapine can be reduced or stopped after 8 weeks if patients are tolerating selinexor.[5,6]

For reference purposes only. All treatment decisions must be individualized and made solely at the discretion of the healthcare professional.

Recommended monitoring & management for nausea/vomiting & dehydration[1]

Fluid intake	IV hydration	Monitor CBC
Ensure patients maintain adequate fluid and caloric intake throughout treatment	Consider IV hydration and replace electrolytes as clinically indicated	Monitor CBC with differential, standard blood chemistries, body weight, nutritional status, and volume status at baseline and during treatment as clinically indicated

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Please see Important Safety Information throughout this brochure, and accompanying full Prescribing Information.

XVd trial design[1]

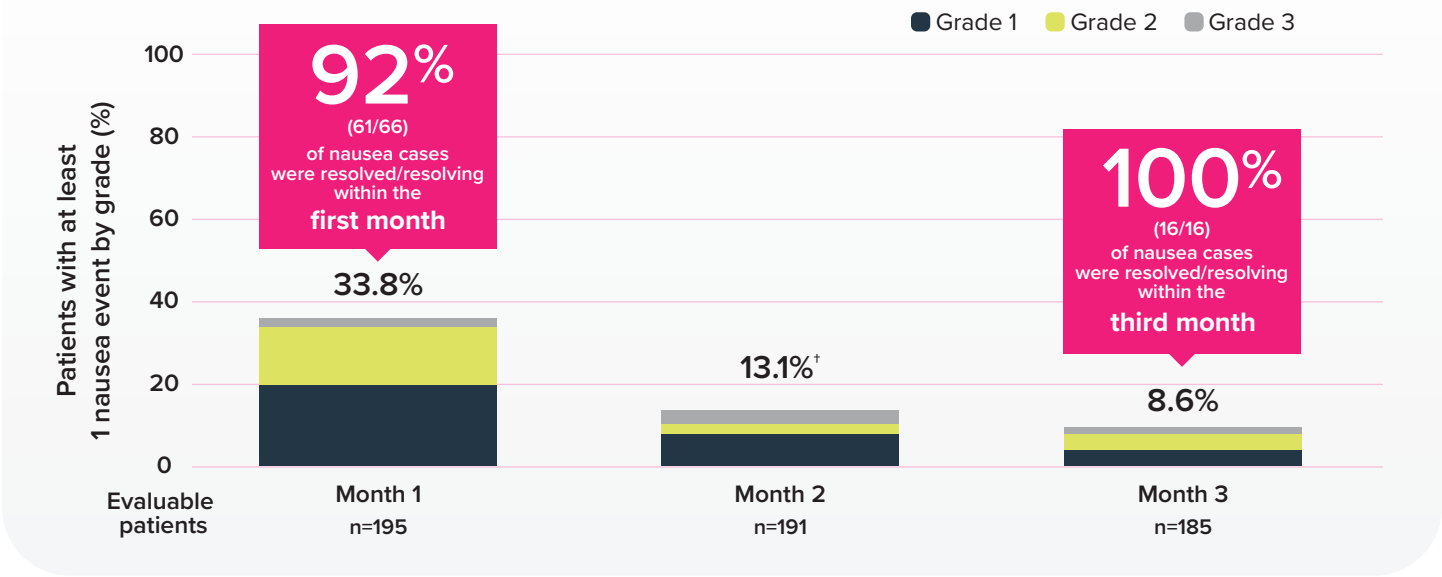
The XVd trial was a phase 3, global, randomized, open-label study of patients with MM who had received 1-3 prior therapies that compared XPOVIO + Vd (XVd) with Vd (bortezomib + dexamethasone). The primary efficacy endpoint was median PFS (mPFS). In the trial, 402 patients were randomized into 2 study arms*:

- 195 patients were treated with once-weekly XPOVIO + bortezomib and twice-weekly dexamethasone
- 207 patients were treated with twice-weekly bortezomib and four-times-weekly dexamethasone

*Randomization was stratified based on prior proteasome inhibitor exposure, number of prior regimens, stage, and region.

In the XVd trial, nausea was transient and reversible[2]

Percentage of patients experiencing nausea events per month in the XVd arm of the XVd trial



†80% (20/25) of cases were resolved/resolving within the second month.

The XVd trial protocol required a prophylactic 5-HT3 antagonist and other anti-nausea treatment agents prior to and during treatment with XPOVIO to address nausea and allowed for other interventions as required.[2]

IMPORTANT SAFETY INFORMATION (cont'd)

Embryo-Fetal Toxicity: XPOVIO can cause 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.

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3 Assess for dose modification

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XPOVIO dosage may be adjusted to help mitigate potential ARs[1]

Recommended XPOVIO dose reduction steps

65% (126/195) of patients in the XVd arm of the XVd trial had an **XPOVIO dose reduction**[2]

80 mg (range 30–137 mg) taken once weekly was the **median dosage of XPOVIO** in the XVd arm[1]

Recommended monitoring & management for select ARs[1]

Thrombocytopenia	Neutropenia	Hyponatremia
Monitor platelet counts at baseline; monitor for bleeding and evaluate promptly; institute platelet transfusion and/or other treatments as clinically indicated	Monitor WBCs with differential at baseline; monitor for infection and evaluate promptly; consider supportive measures including antimicrobials and growth factors	Monitor sodium levels at baseline and correct sodium levels for concurrent hyperglycemia and high serum paraprotein levels; assess hydration status and manage hyponatremia per clinical guidelines

Please see the recommended dosage modification guidelines and additional considerations in the full Prescribing Information.

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.

Please see Important Safety Information throughout this brochure, and accompanying full Prescribing Information.

In the XVd trial, efficacy was maintained with XPOVIO dose reductions[1,2,12]

ITT Population

XVd arm
13.9 months mPFS
(n=195, 95% CI: 11.7, NE)

Vd arm*
9.5 months mPFS
(n=207, 95% CI: 7.6, 10.8)

*The Vd (bortezomib plus dexamethasone) cohort did not receive XPOVIO

XPOVIO Dose Reduction in the XVd arm†

Dose reduction
16.6 months mPFS
(n=126, 95% CI: 12.9, NE)

No dose reduction
9.2 months mPFS
(n=69, 95% CI: 6.77, 15.47)

†mPFS in patients with XPOVIO dose reduction to help mitigate adverse reactions

Limitations of post hoc analysis:

- This post hoc analysis is exploratory in nature and was not a study objective
- This post hoc analysis was underpowered to detect clinically meaningful differences in treatment effect
- This post hoc analysis was intended to provide information about dose modifications and not to compare efficacy across treatment groups

XPOVIO dose reduction: incidence of duration-adjusted ARs[12‡]

Adverse reactions (%)	On or before first XPOVIO dose reduction (n=195)		After first XPOVIO dose reduction (n=126)	
	All grades	Grade ≥3	All grades	Grade ≥3
Thrombocytopenia	62.5	29.6	47.6	19.2
Nausea	31.6	3.9	7.3	2.7
Fatigue	28.1	4.1	9.9	2.7
Decreased appetite	21.5	1.6	6.4	0.4
Anemia	17.9	4.7	10.3	3.2
Diarrhea	12.9	2.0	5.2	0.7
Neutropenia	10.6	4.0	7.7	4.8
Weight decreased	9.0	0.6	5.9	0.7

‡Duration-adjusted incidence of ARs is defined as the average number of events per 100 patients during a 4-week cycle.

ADVERSE REACTIONS (cont'd)

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.

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4 Connect patients with additional support

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KaryForward Patient Support Program

KaryFORWARD® PATIENT SUPPORT BY KARYOPHARM

Enroll Patients in KaryForward® — a patient support program dedicated to providing assistance and resources to patients and their caregivers

- **Insurance Verification**
- **Financial Assistance***
- **Dose Exchange Program**
- **Additional Support and Resources**

*All programs and support are subject to eligibility requirements.

Enroll your patients or learn more: **CALL** 1-877-KARY4WD (1-877-527-9493) Monday through Friday, 8 AM to 8 PM ET or **VISIT** KaryForward.com/hcp

Scan to access the KaryForward HCP website

Patient support materials

Provide the below patient support materials to educate patients about what to expect when starting XPOVIO

Treatment Experience Guide for Patients and Caregivers
Educational tool with useful tips that helps patients understand what to expect when starting treatment.

Patient Starter Kit
Contains helpful resources for patients starting on XPOVIO, including a cookbook with cancer-friendly recipes.

Contact your local Karyopharm® Representative or enroll your patients in the KaryForward® Patient Support Program to ensure your patients receive these helpful resources.

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.

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Abbreviations: 5-HT3, 5-hydroxytryptophan receptor; 5-HT2, 5-hydroxytryptophan receptor 2A; AR, adverse reaction; CBC, complete blood count; CI, confidence interval; CL_{CR}, creatinine clearance; D2, dopamine receptor 2; G-CSF, granulocyte colony-stimulating factor; ITT, intent to treat; IV, intravenous; NE, not evaluable; NK-1, neurokinin receptor; PFS, progression-free survival; mPFS; median progression-free survival; WBC, white blood cell; XVd, selinexor, bortezomib, and dexamethasone.

References: 1. XPOVIO® [prescribing information]. Newton, MA: Karyopharm Therapeutics Inc.; **2.** Data on file. Karyopharm Therapeutics Inc. 2021; **3.** Colson K. *Support Care Cancer*. 2015;23(5):1431–1445; **4.** Kurtin S. *Semin Oncol Nurs*. 2017;33(3):348–361; **5.** Gavriatopoulou M, et al. *Leukemia*. 2020;34(9):2430-2440; **6.** Mikhael J, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(6):351-357; **7.** Chari A, et al. *Clin Lymphoma Myeloma Leuk*. 2021;21(12):e975-e984; **8.** ZOFRAN® [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; **9.** Saudemont G, et al. *BMC Palliat Care*. 2020;19(1):56; **10.** EMEND® [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc; **11.** VARUBI® [prescribing information]. Deerfield, IL: TerSera Therapeutics LLC; **12.** Jagannath S, et al. Poster presented at: 63rd ASH Annual Meeting and Exposition; December 13, 2021; Atlanta, GA.

Karyopharm® Therapeutics