XPOVIO® (selinexor)

Multiple Myeloma Patient Management Guide

A detailed guide to help:

Get patients started on XPOVIO® (selinexor)

- Set treatment expectations
- Proactively manage nausea

Assess for dose modification

- Modify the dose of XPOVIO to mitigate specific adverse reactions (ARs)

Connect patients with additional support

- Enroll eligible 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.

Please see Important Safety Information throughout and full Prescribing Information.

SECTION 1

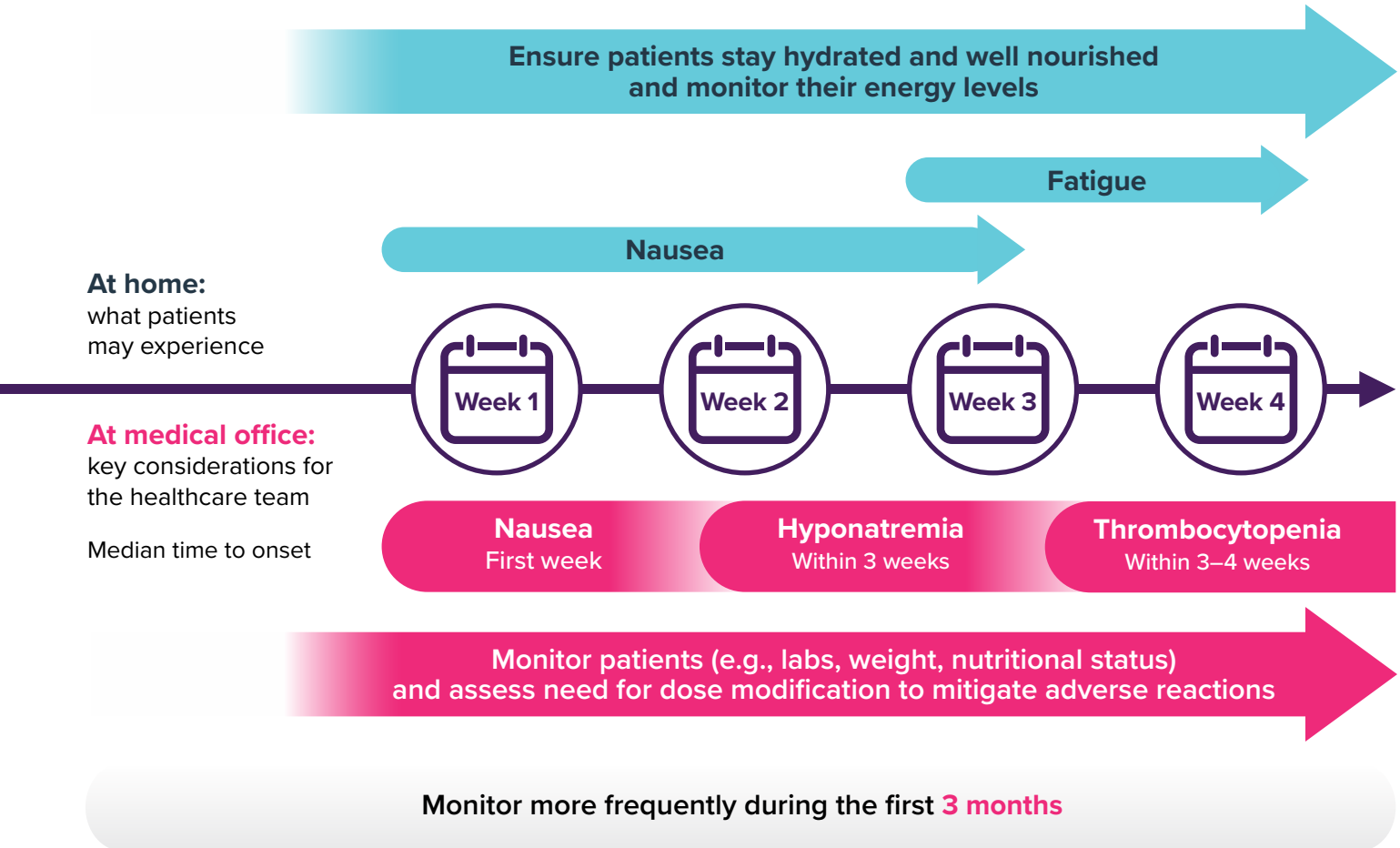
Get patients started on XPOVIO®

XPOVIO® (selinexor)

For patients who have relapsed/refractory multiple myeloma, XPOVIO provides an opportunity to introduce a different drug class to help treat their disease. Familiarity with some key considerations can be helpful before starting and managing patients on XPOVIO, especially in their first month of treatment.

Set treatment expectations

Considerations when starting a patient on XPOVIO[1]



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

For more detailed information on starting patients on XPOVIO, please see the Getting Patients Started Guide.

IMPORTANT SAFETY INFORMATION (continued)

Thrombocytopenia (cont): 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 and full Prescribing Information.

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Recommended dosing schedule[1]

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
 **XPOVIO 100 mg** + **bortezomib 1.3 mg/m²** for first 4 weeks, followed by 1 week off + **dexamethasone 20 mg**	**Dexamethasone 20 mg**	No dose	No dose	No dose	No dose	No dose
Recommended prophylactic antiemetics*[2,3]						
Ondansetron 8 mg 30 minutes prior to XPOVIO then Q8 hours + **Olanzapine** 2.5–5 mg QHS	**Ondansetron** 8 mg Q8 hours + **Olanzapine** 2.5–5 mg QHS	**Ondansetron** 8 mg Q8 hours + **Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS	**Olanzapine** 2.5–5 mg QHS

*An NK-1 antagonist (e.g., aprepitant or rolapitant) could also be used as an antiemetic. Antiemetics such as olanzapine and NK-1 inhibitors can be reduced or stopped after 8 weeks if patients are tolerating XPOVIO.

The specific antiemetics listed above are for reference purposes only. All treatment decisions must be individualized and made solely at the discretion of the healthcare professional.

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

How to take XPOVIO[1]

- Each XPOVIO dose should be taken at approximately the same time of day
- Each tablet should be swallowed whole with water
- Do not break, chew, crush, or divide the tablets
- If a dose of XPOVIO is missed or delayed, instruct patients to take their next dose at the next regularly scheduled time
- If a patient vomits following a dose of XPOVIO, the patient should not repeat the dose and should take the next dose on the next regularly scheduled day
- Advise patients that XPOVIO comes in a child-resistant blister pack
- Advise patients to take their prescribed dexamethasone (if applicable) and prophylactic anti-nausea medications as directed
- Advise patients to maintain appropriate fluid and caloric intake throughout their treatment

IMPORTANT SAFETY INFORMATION (continued)

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.

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Proactively manage nausea

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

5-HT3 antagonist[1]

e.g., Ondansetron

8 mg taken orally 30 minutes prior to each dose of XPOVIO and scheduled for Q8 hours for 2 days following dosing[2,3]

+

D2 & 5-HT2A antagonist[2,3]

e.g., Olanzapine

2.5 mg–5 mg taken orally QHS

NK-1 antagonists (e.g., aprepritant or rolapitant) can be used in place of a D2/5-HT2A antagonist. Antiemetics such as NK-1 inhibitors and olanzapine can be reduced or stopped after 8 weeks if patients are tolerating XPOVIO.[2,3]

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

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

Fluid intake	Intravenous (IV) hydration	Monitor CBC and health status
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, and more frequently during the first 3 months of treatment

See page 8 and page 9 for detailed information on dose modification for XPOVIO-associated nausea.

IMPORTANT SAFETY INFORMATION (continued)

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 and full Prescribing Information.

SECTION 2

Assess for dose modification

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Four dosage strengths are available for dose modifications to help mitigate adverse reactions[1]

100 mg
RECOMMENDED STARTING DOSE

80 mg
FIRST REDUCTION

60 mg
SECOND REDUCTION

40 mg
THIRD REDUCTION

PERMANENTLY DISCONTINUE

Detailed SKU information for once-weekly XVd dose modifications

NDC	Contents	Tablets/blister pack	Weekly dose	Carton
NDC 72237-103-05	Four blister packs (eight tablets total in the carton)	Two 50-mg tablets	**100 mg once weekly**	
NDC 72237-102-02	Four blister packs (eight tablets total in the carton)	Two 40-mg tablets	**80 mg once weekly**	
NDC 72237-104-01	Four blister packs (four tablets total in the carton)	One 60-mg tablet	**60 mg once weekly**	
NDC 72237-102-07	Four blister packs (four tablets total in the carton)	One 40-mg tablet	**40 mg once weekly**	

IMPORTANT SAFETY INFORMATION (continued)

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.

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XVd Trial Design[1]

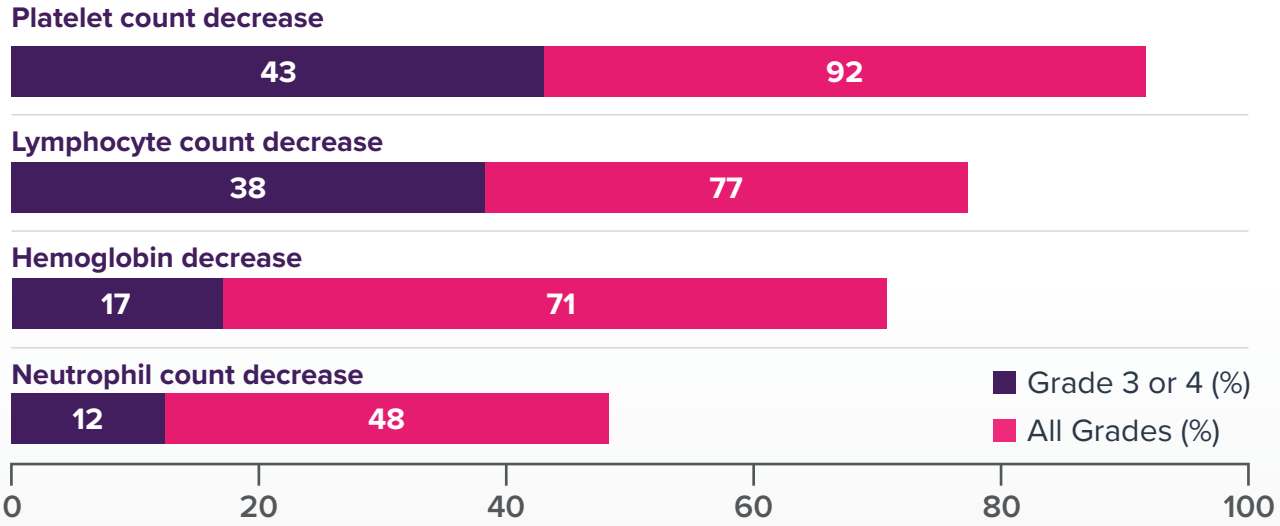
The XVd trial was a phase 3, global, randomized, open-label study of patients with MM who had received 1-3 prior therapies that compared XPOVIO + Vd (XVd) with Vd (bortezomib + dexamethasone). The primary efficacy endpoint was median PFS (mPFS). In the trial, 402 patients were randomized into 2 study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

Hematologic adverse reactions[1]

Select laboratory abnormalities that worsened from baseline (incidence ≥15%)[1]



The denominator used to calculate the rate varied from 91 to 201 based on the number of patients with at least one post-treatment value.

Thrombocytopenia

- The median time to first onset of thrombocytopenia was 22 days for any grade and 43 days for Grade 3 or 4. Bleeding occurred in 16% of patients with thrombocytopenia, clinically significant bleeding (Grade ≥3) occurred in 4% of patients with thrombocytopenia, and fatal hemorrhage occurred in 2% of patients with thrombocytopenia. Permanent discontinuation of XPOVIO due to thrombocytopenia occurred in 2% of patients.
- 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 the severity of adverse reaction

IMPORTANT SAFETY INFORMATION (continued)

Hyponatremia: XPOVIO can cause severe or life-threatening hyponatremia. Monitor sodium level at baseline and throughout treatment.

Please see Important Safety Information throughout and full Prescribing Information.

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Hematologic adverse reactions[1] (cont)

Neutropenia

- The median time to first onset of neutropenia was 23 days for any grade and 40 days for Grade 3 or 4
- Febrile neutropenia was reported in <1% of patients
- Obtain white blood cell counts with differential at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment
- Monitor patients for signs and symptoms of concomitant infection and evaluate promptly
- Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF)
- Interrupt, reduce dose, or permanently discontinue based on the severity of adverse reaction

Dosage modification guidelines for hematologic adverse reactions[1]

	Occurrence	Action
Thrombocytopenia		
Platelet count 25,000 to <75,000/µL	Any	• Reduce XPOVIO by one dose level
Platelet count 25,000 to <75,000/µL *with* concurrent bleeding	Any	• Interrupt XPOVO • Restart XPOVIO at one dose level lower after bleeding has resolved • Administer platelet transfusions per clinical guidelines
Platelet count <25,000/µL	Any	• Notifications found in terms of Sutton Interrupt XPOVIO • Monitor until platelet count returns to at least 50,000/µL • Restart XPOVIO at one dose level lower
Neutropenia		
Absolute neutrophil count of 0.5 to 1 x 10^9/L *without* fever	Any	• Reduce XPOVIO by one dose level
Absolute neutrophil count less than 0.5 x 10^9/L *OR* febrile neutropenia	Any	• Interrupt XPOVO • Monitor until neutrophil count returns to ≥1 x 10^9/L • Restart XPOVIO at one dose level lower
Anemia		
Hemoglobin <8 g/dL	Any	• Reduce XPOVIO by one dose level • Administer blood transfusions per clinical guidelines
Life-threatening consequences	Any	• Interrupt XPOVIO • Monitor hemoglobin until levels return to ≥8 g/dL • Restart XPOVIO at one dose level lower • Administer blood transfusions per clinical guidelines

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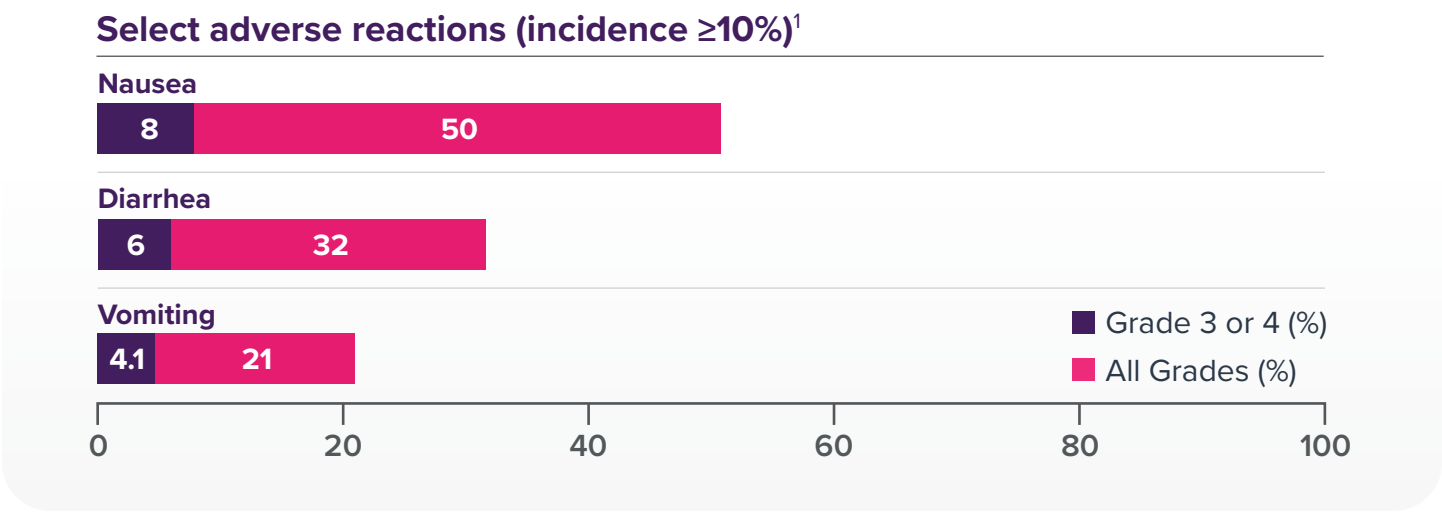
Gastrointestinal adverse reactions[1]



Nausea/vomiting

- The median time to onset of the first nausea event and vomiting was 6 and 8 days, respectively
- Interrupt, reduce dose, or permanently discontinue based on the severity of adverse reaction Administer IV fluids to prevent dehydration and replace electrolytes as clinically indicated
- Permanent discontinuation due to nausea occurred in 3.1% of patients and due to vomiting occurred in 2.1% of patients
- Provide prophylactic antiemetics. Administer a 5-HT3 receptor antagonist and other anti-nausea agents prior to and during treatment with XPOVIO

Diarrhea

- he median time to onset of diarrhea was 50 days
- Permanent discontinuation due to diarrhea occurred in 1% of patients
- Interrupt, reduce dose, or permanently discontinue based on the severity of adverse reaction
- Provide standard antidiarrheal agents, administer IV fluids to prevent dehydration, and replace electrolytes as clinically indicated

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Dosage modification guidelines for gastrointestinal adverse reactions[1]

	Occurrence	Action
Nausea and vomiting		
Grade 1 or 2 nausea (oral intake decreased without significant weight loss, dehydration, or malnutrition) OR Grade 1 or 2 vomiting (≤5 episodes per day)	Any	• Maintain XPOVIO and initiate additional antinausea medications
Grade 3 nausea (inadequate oral caloric or fluid intake) OR Grade ≥3 vomiting (≥6 episodes per day)	Any	• Interrupt XPOVIO • Monitor until nausea or vomiting has resolved to Grade ≤2 or baseline • Initiate additional antinausea medications • Restart XPOVIO at one dose level lower
Diarrhea		
Grade 2 (increase of 4–6 stools/day over baseline)	1st	• Maintain XPOVIO and institute supportive care
	2nd and subsequent	• Reduce XPOVIO by one dose level • Institute supportive care
Grade ≥3 (≥7 stools/day over baseline; hospitalization indicated)	Any	• Interrupt XPOVIO and institute supportive care • Monitor until diarrhea resolves to Grade ≤2 • Restart XPOVIO at one dose level lower

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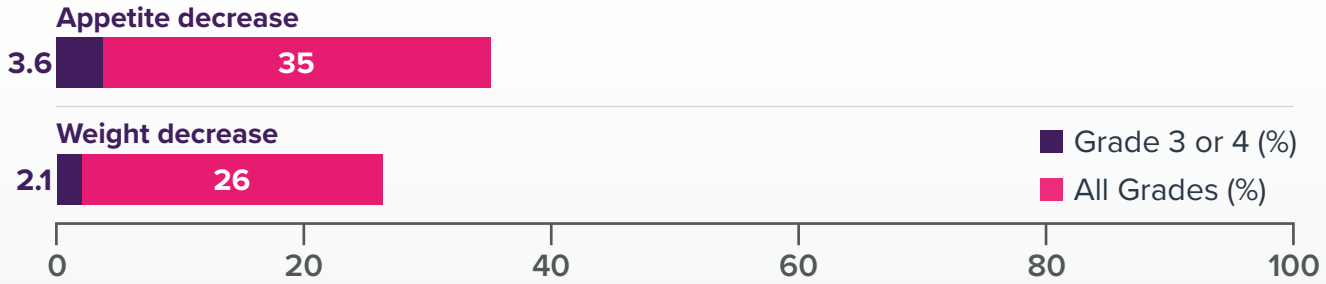
Select metabolism and nutrition adverse reactions[1]

Select laboratory abnormality (incidence ≥15%)[1]

The denominator used to calculate the rate was 195 based on the number of patients with at least one post-treatment value.

Select adverse reactions (incidence ≥10%)[1]



Hyponatremia

- The median time to first onset was 21 and 22 days for any grade and Grade 3 or 4 hyponatremia, respectively
- Monitor sodium level at baseline and throughout treatment. Monitor more frequently during the first 2 months of treatment
- Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels
- Assess hydration status and manage hyponatremia per clinical guidelines, including IV saline and/or salt tablets as appropriate and dietary review. Interrupt, reduce dose, or permanently discontinue based on the severity of the adverse reaction

Weight loss and anorexia

- Median time to weight loss and anorexia was 58 and 35 days, respectively
- Permanent discontinuation due to anorexia occurred in 2.1% of patients and due to weight loss occurred in 1% of patients
- Monitor weight, nutritional status, and volume status at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment
- Interrupt, reduce dose, or permanently discontinue based on the severity of the adverse reaction
- Provide nutritional support, fluids, and electrolyte repletion as clinically indicated

IMPORTANT SAFETY INFORMATION (continued)

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 and full Prescribing Information.

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Dosage modification guidelines for metabolism and nutrition adverse reactions[1]

	Occurrence	Action
Hyponatremia		
Sodium level ≤130 mmol/L	Any	• Interrupt XPOVIO, evaluate, and provide supportive care • Monitor until sodium levels return to >130 mmol/L • Restart XPOVIO at one dose level lower
Weight loss and anorexia		
Weight loss of 10% to <20% OR Anorexia associated with significant weight loss or malnutrition	Any	• Interrupt XPOVO and institute supportive care • Monitor until weight returns to >90% of baseline weight • Restart XPOVIO at one dose level lower

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Infections[1]

Select adverse reaction (incidence ≥10%)[1]

[a]Upper respiratory tract infection includes upper respiratory infection, nasopharyngitis, pharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis, and viral upper respiratory tract infection.

- In total, 69% of patients receiving XPOVIO experienced any grade of infection
- Grade ≥3 infections were reported in 32% of patients, and deaths from infections occurred in 3.1% of patients
- The most frequently reported Grade ≥3 infection was pneumonia in 14% of patients, followed by sepsis in 4.1% and upper respiratory tract infection in 3.6% of patients
- Atypical infections reported after XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection
- Monitor for signs and symptoms of infection, evaluate, and treat promptly

IMPORTANT SAFETY INFORMATION (continued)

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.

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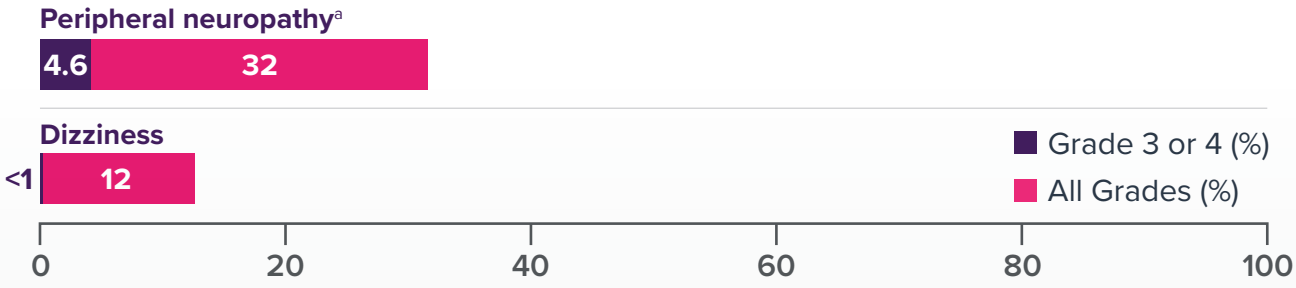
Neurological toxicity[1]

Select adverse reaction (incidence ≥10%)[1]



[a]Peripheral neuropathy includes peripheral neuropathy, peripheral sensory neuropathy, polyneuropathy, peripheral sensorimotor neuropathy, toxic neuropathy, and peripheral motor neuropathy.

- The median time to the first event was 29 days
- Neurological adverse reactions (excluding peripheral neuropathy), including dizziness, syncope, depressed level of consciousness, vertigo, amnesia, and mental status changes (including delirium and confusional state), occurred in 26% of patients, and severe events (Grade 3 or 4) occurred in 3.6% of patients
- Permanent discontinuation due to neurological adverse reactions occurred in 2.1% of patients
- 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, such as operating heavy or potentially dangerous machinery, until the neurological toxicity fully resolves
- Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes. Institute fall precautions as appropriate

IMPORTANT SAFETY INFORMATION (continued)

Cataracts: 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.

Please see Important Safety Information throughout and full Prescribing Information.

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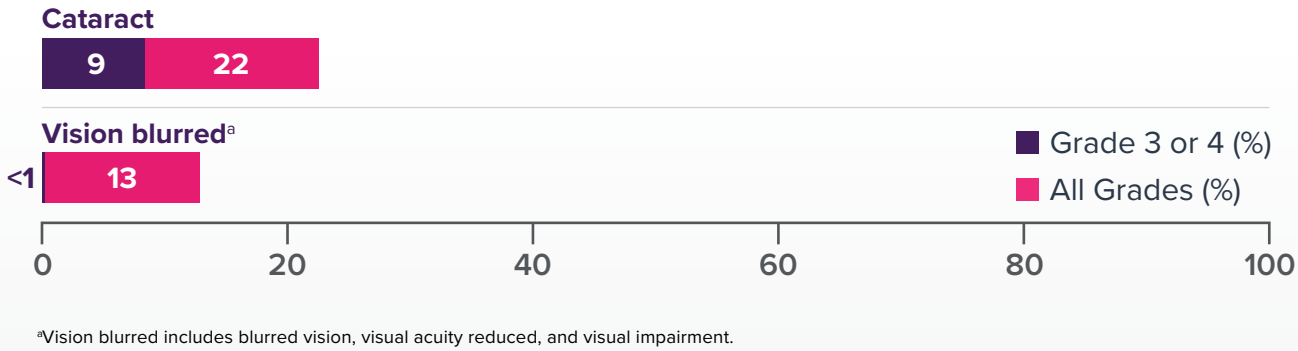
Ocular toxicity[1]

Select adverse reactions (incidence ≥10%)[1]



[a]Vision blurred includes blurred vision, visual acuity reduced, and visual impairment.

Cataract

- The median time to new onset of cataract was 228 days and was 237 days for worsening of cataract in patients presenting with cataract at start of XPOVIO therapy
- Treatment of cataracts usually requires surgical removal of the cataract

Dosage modification guidelines for ocular toxicity[1]

	Occurrence	Action
Ocular toxicity		
Grade 2, excluding cataract	Any	• Perform opthalmologic evaluation • Interrupt XPOVIO and provide supportive care • Monitor until ocular symptoms resolve to Grade 1 or baseline • Restart XPOVIO at one dose level lower
Grade ≥3, excluding cataract	Any	• Permanently discontinue XPOVIO • Perform ophthalmologic evaluation

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.

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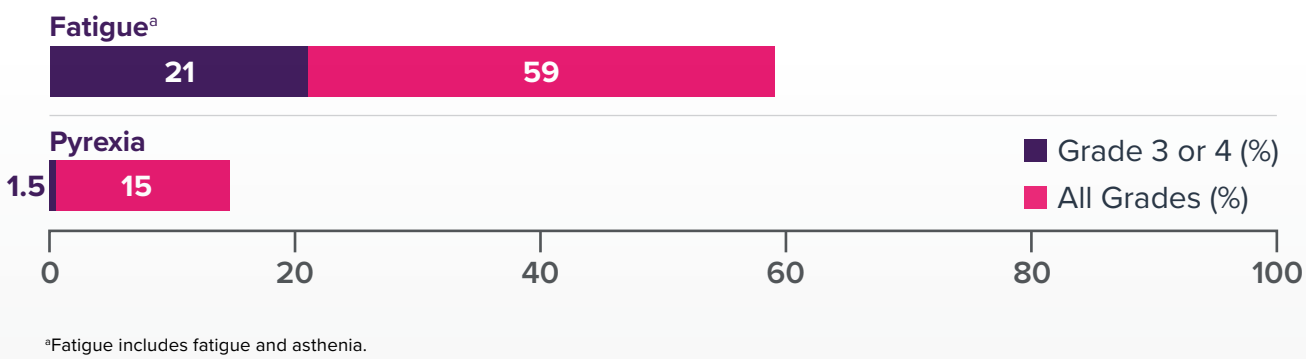
Fatigue and other adverse reactions[1]

Select adverse reactions (incidence ≥10%)[1]



[a]Fatigue includes fatigue and asthenia.

Dosage modification guidelines for fatigue and other adverse reactions[1]

	Occurrence	Action
Fatigue		
Grade 2 lasting >7 days OR Grade 3	Any	• Interrupt XPOVIO • Monitor until fatigue resolves to Grade 1 or baseline • Restart XPOVIO at one dose level lower
Other non-hematologic adverse reactions		
Grade 3 or 4	Any	• Interrupt XPOVIO • Monitor until resolved to Grade ≤2 • Restart XPOVIO at one dose level lower

ADVERSE REACTIONS (continued)

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.

Please see Important Safety Information throughout and full Prescribing Information.

SECTION 3

Connect eligible patients with additional support

XPOVIO® (selinexor)

KaryForward® Patient Support Program

KaryFORWARD®
PATIENT SUPPORT BY KARYOPHARM

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

- Insurance Coverage Process
- Financial Assistance*
- Dose Exchange Program
- Support from Nurse Case Managers

*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 eligible 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.

Please see Important Safety Information throughout and 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.

Abbreviations: 5-HT2A, serotonin receptor 2A; 5-HT3, serotonin receptor 3; ARs, adverse reactions; CBC, complete blood count; CL_{CR}, creatinine clearance; D2, dopamine receptor 2; G-CSF, granulocyte colony stimulating factor; HCP, healthcare provider; IV, intravenous; NDC, national drug code; NK-1, neurokinin 1; Q, every; QHS, at night.

References: 1. XPOVIO® [prescribing information]. Newton, MA: Karyopharm Therapeutics, Inc.; **2.** Gavriatopoulou M, et al. *Leukemia*. 2020;34(9):2430–2440; **3.** Mikhael J, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(6): 351–357.

Karyopharm® Therapeutics