XPOVIO® (selinexor)

THE X FACTOR

In multiple myeloma

RESTORE YOUR PATIENTS' OWN CANCER DEFENSES

A DOSING AND DOSAGE MODIFICATION GUIDE XPOVIO + Vd (XVd)

XPOVIO is the first and only FDA-approved XPO1 inhibitor that helps restore the body's own tumor suppressor pathways to fight multiple myeloma (MM) as early as first relapse[1]

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.

Please see full Prescribing Information.

Getting patients started[1]

1. Set expectations

- Counsel patients on what to expect with XPOVIO® (selinexor) therapy
- Advise patients to maintain adequate fluid and caloric intake throughout treatment

2. Prescribe XPOVIO

- XPOVIO is taken orally on Day 1 of each week
- During therapy with XPOVIO, refer to instructions for antiemetics on page 8

3. Monitor your patient

- During therapy with XPOVIO, provide additional antiemetics as needed
- Monitor complete blood count (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
- Consider intravenous hydration for patients at risk of dehydration
- Assess the need for dose modifications

Recommended weekly dosage and schedule[1]

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
 **XPOVIO 100 mg** + bortezomib 1.3 mg/m² + dexamethasone 20 mg	dexamethasone 20 mg	**No dose**	**No dose**	**No dose**	**No dose**	**No dose**

 = 50 mg

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:

- 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 each week

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

Beginning treatment with XPOVIO[1]

XPOVIO® (selinexor)

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 a dose of XPOVIO, the patient should not repeat the dose, and the patient 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 and prophylactic antinausea medications exactly as prescribed.
- Appropriate fluid and caloric intake should be maintained throughout treatment.

SELINEXOR (XPOVIO) IS RECOMMENDED BY THE NCCN GUIDELINES® IN ONCOLOGY AS A CATEGORY 1* THERAPEUTIC OPTION IN PREVIOUSLY TREATED MM[2]

*Category 1=Based upon high-level evidence, there is uniform National Comprehensive Cancer Network® (NCCN®) consensus that the intervention is appropriate. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.7.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved.[2]

Please see full Prescribing Information.

Monitoring and managing adverse reactions (ARs)[1]

Monitoring for ARs[1]

Monitor complete blood count (CBC) with differential, standard blood chemistries, body weight, nutritional status, and volume status at baseline and during treatment as clinically indicated.

Monitor more frequently during the first 3 months of treatment.

Assess the need for dosage modifications of XPOVIO® (selinexor) due to adverse reactions.

Recommended concomitant treatments[1]

During therapy with XPOVIO, refer to instructions for antiemetics on page 8

Advise patients to maintain adequate fluid and caloric intake throughout treatment.

Consider intravenous hydration for patients at risk of dehydration.

Please refer to page 19 for how XPOVIO is supplied.

Dose modification[1]

XPOVIO® (selinexor)

Dosage reduction steps for ARs[1]

Recommended starting dosage	100 mg

	DOSE REDUCTION
First reduction	80 mg
Second reduction	60 mg
Third reduction	40 mg
Fourth reduction	PERMANENTLY DISCONTINUE

Hematologic adverse reactions (ARs)[1]

Laboratory Abnormality (incidence ≥15%)[1]	Grade 3 or 4 %	All Grades %
Platelet count decrease	43	92
Lymphocyte count decrease	38	77
Hemoglobin decrease	17	71
Neutrophil count decrease	12	48

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[1]

- 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 occurred in 4% of patients with thrombocytopenia, and fatal hemorrhage occurred in 2% of patients with thrombocytopenia
- 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[1]

- 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 severity of adverse reaction

Dosage modification guidelines for hematologic ARs[1]

XPOVIO® (selinexor)

Thrombocytopenia[1]		
AR	**Occurrence**	**Action**
Platelet count 25,000 to <75,000/mcL	Any	• Reduce XPOVIO® (selinexor) by 1 dose level
Platelet count 25,000 to <75,000/mcL *with* concurrent bleeding	Any	• Interrupt XPOVIO • Restart XPOVIO at 1 dose level lower after bleeding has resolved • Administer platelet transfusions per clinical guidelines
Platelet count <25,000/mcL	Any	• Interrupt XPOVIO • Monitor until platelet count returns to ≥50,000/mcL • Restart XPOVIO at 1 dose level lower
Neutropenia[1]		
AR	**Occurrence**	**Action**
Absolute neutrophil count of 0.5 to 1 x 10^9/L without fever	Any	• Reduce XPOVIO by 1 dose level
Absolute neutrophil count <0.5 x 10^9/L *OR* Febrile neutropenia	Any	• Interrupt XPOVIO • Monitor until neutrophil counts return to ≥1 x 10^9/L • Restart XPOVIO at 1 dose level lower
Anemia[1]		
AR	**Occurrence**	**Action**
Hemoglobin <8 g/dL	Any	• Reduce XPOVIO by 1 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 1 dose level lower • Administer blood transfusions per clinical guidelines

Please see full Prescribing Information.

Gastrointestinal adverse reactions (ARs)[1]

Adverse Reactions (incidence ≥10%)[1]	Grade 3 or 4 %	All Grades %
Nausea	8	50
Diarrhea	6	32
Vomiting	4.1	21

Nausea/Vomiting[1]

- 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 severity of adverse reaction. Administer intravenous fluids to prevent dehydration and replace electrolytes as clinically indicated

Double antinausea coverage[1]

- Ondansetron 8 mg PO[3] 30 to 60 minutes prior to each dose and continued for every 8 hours for 2 days following dosing **AND**
  - Olanzapine 2.5 mg–5.0 mg PO qhs[4] **OR**
  - Aprepitant 125 mg PO QAM day 1 and 80 mg for 2 days each week[3,5,6*] **OR**
  - Rolapitant 180 mg PO 2 hours before XPOVIO Q2W[3,7]
- Alternatively, once weekly oral dose of Akynzeo (netupitant 300 mg + palonosetron 0.5 mg)[8,9]
- One or both antiemetics may be tapered after 8 weeks of therapy[3]

*If using aprepitant, the dose of dexamethasone may need to be reduced.

Diarrhea[1]

- Median time to onset of diarrhea was 50 days
- Provide standard antidiarrheal agents, administer intravenous fluids to prevent dehydration, and replace electrolytes as clinically indicated
- Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction

Dosage modification guidelines for gastrointestinal ARs[1]

XPOVIO® (selinexor)

Nausea and Vomiting[1]		
AR	**Occurrence**	**Action**
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® (selinexor) 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 1 dose level lower

Diarrhea[1]		
AR	**Occurrence**	**Action**
Grade 2 (increase of 4 to 6 stools per day over baseline)	1st	• Maintain XPOVIO and institute supportive care
	2nd and subsequent occurrences	• Reduce XPOVIO by 1 dose level • Institute supportive care
Grade ≥3 (≥7 stools per day over baseline; hospitalization indicated)	Any	• Interrupt XPOVIO and institute supportive care • Monitor until diarrhea resolves to Grade ≤2 • Restart XPOVIO at 1 dose level lower

Metabolism and nutrition adverse reactions (ARs)[1]

Laboratory Abnormality (incidence ≥15%)[1]	Grade 3 or 4 %	All Grades %
Sodium decrease	14	58

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.

Adverse Reactions (incidence ≥10%)[1]	Grade 3 or 4 %	All Grades %
Appetite decrease	3.6	35
Weight decrease	2.1	26

Hyponatremia[1]

- The median times to first onset was 21 days and 22 days for Grade 3 or 4
- 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 intravenous saline and/or salt tablets as appropriate and dietary review. Interrupt, reduce dose, or permanently discontinue based on severity of the adverse reaction

Weight loss and anorexia[1]

- Median time to weight loss and anorexia was 58 and 35 days, respectively
- 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 severity of the AR
- Provide nutritional support, fluids, and electrolyte repletion as clinically indicated

Dosage modification guidelines for hyponatremia, anorexia, and weight loss[1]

XPOVIO® (selinexor)

Hyponatremia[1]		
AR	**Occurrence**	**Action**
Sodium level ≤130 mmol/L	Any	• Interrupt XPOVIO® (selinexor), evaluate, and provide supportive care • Monitor until sodium levels return to >130 mmol/L • Restart XPOVIO at 1 dose level lower

Weight Loss and Anorexia[1]		
AR	**Occurrence**	**Action**
Weight loss of 10% to <20% *OR* Anorexia associated with significant weight loss or malnutrition	Any	• Interrupt XPOVIO and institute supportive care • Monitor until weight returns to >90% of baseline weight • Restart XPOVIO at 1 dose level lower

Infections[1]

Adverse Reactions (incidence ≥10%)[1]	Grade 3 or 4 %	All Grades %
Upper respiratory tract infection[a]	3.6	29

[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.

- 69% of patients receiving XPOVIO® (selinexor) 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

Neurological toxicity[1]

XPOVIO® (selinexor)

Adverse Reactions (incidence ≥10%)[1]	Grade 3 or 4 %	All Grades %
Peripheral neuropathy (PN)[a]	4.6	32
Dizziness	<1	12

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

- Median time to the first event was 29 days
- Neurological ARs (excluding PN) 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
- 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

Ocular toxicity[1]

Adverse Reactions (AR) (incidence ≥10%)[1]	Grade 3 or 4 %	All Grades %
Cataract	9	22
Vision blurred[a]	<1	13

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

Cataract[1]

- 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® (selinexor) therapy

Dosage modification guidelines for ocular toxicity[1]

XPOVIO® (selinexor)

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

Fatigue and other ARs[1]

Adverse Reactions (incidence ≥10%)[1]	Grade 3 or 4 %	All Grades %
Fatigue[a]	28	59
Pyrexia	1.5	15

[a]Fatigue includes fatigue and asthenia.

- The NCCN recommends considering psychostimulants, such as methylphenidate, after ruling out other causes of fatigue[10*]

  Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Related Fatigue V.1.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved.[10]

  *Pharmacologic interventions remain investigational, but have been reported to improve symptoms of fatigue in some patients. Methylphenidate should be used cautiously and should not be used until treatment- and disease-specific morbidities have been characterized or excluded.

Dosage modification guidelines for fatigue and other ARs[1]

XPOVIO® (selinexor)

Fatigue[1]		
AR	**Occurrence**	**Action**
Grade 2 lasting >7 days *OR* Grade 3	Any	• Interrupt XPOVIO® (selinexor) • Monitor until fatigue resolves to Grade 1 or baseline • Restart XPOVIO at 1 dose level lower
Other Non-hematologic ARs[1]		
AR	**Occurrence**	**Action**
Grade 3 or 4	Any	• Interrupt XPOVIO • Monitor until resolved to Grade ≤2, restart XPOVIO at 1 dose level lower

Use in patients ≥65, patients with renal disease, and pregnant women[1]

- No overall difference in effectiveness of XPOVIO® (selinexor) 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
- XPOVIO can cause fetal harm when administered to a pregnant woman
- Advise pregnant women of the potential risk to a fetus. There is no information regarding the presence of selinexor or its metabolites in human milk, or their effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with XPOVIO and for 1 week after the last dose. 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

SELECTED SAFETY INFORMATION

- The most common ARs (≥20%) 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.
- The treatment discontinuation rate due to ARs was 19%; 64% of patients had a reduction in the XPOVIO dose, and 83% had the dose of XPOVIO interrupted.

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.

Product information

XPOVIO® (selinexor)

PRODUCT NAME
XPOVIO® (selinexor) tablets, for oral use

DISTRIBUTED AND MARKETED BY
Karyopharm Therapeutics® Inc.

HOW SUPPLIED

NDC	Contents	Tablets per blister pack	Weekly dose	Carton
NDC 72237-103-05	4 blister packs (8 tablets total in the carton)	Two 50-mg tablets	**100 mg once weekly**	
NDC 72237-102-02	4 blister packs (8 tablets total in the carton)	Two 40-mg tablets	**80 mg once weekly**	
NDC 72237-104-01	4 blister packs (4 tablets total in the carton)	One 60-mg tablet	**60 mg once weekly**	
NDC 72237-102-07	4 blister packs (4 tablets total in the carton)	One 40-mg tablet	**40 mg once weekly**	

KaryFORWARD®
PATIENT SUPPORT BY KARYOPHARM

XPOVIO®
(selinexor)

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

Insurance coverage

Get assistance navigating the insurance process, including benefits investigations, claims assistance, prior authorizations, and appeals.

- **Quick Start Program:** Gain rapid access to XPOVIO for patients who experience a delay in insurance coverage
- **Bridge Program:** Get an emergency supply of free XPOVIO for patients who experience an unexpected disruption in therapy

Financial assistance

Gain access to programs that can help your eligible patients with the cost of Karyopharm medications.

- **Patient Assistance Program:** Patients who are uninsured or underinsured may be eligible to receive XPOVIO at no cost
- **XPOVIO Copay Program:** Patients with commercial insurance may be eligible to pay as little as $5 for each XPOVIO prescription

Support and resources

Dedicated Nurse Case Managers can provide additional information about XPOVIO treatment such as:

- Prescription instructions
- Psychosocial support and additional nonclinical education
- Highlight what to expect when taking Karyopharm medications and the importance of talking to healthcare providers about the treatment journey
- Determine if additional third-party support is available, such as transportation assistance

Dose exchange program

- Get support for your patients who may need a dose adjustment mid-cycle
- Download the enrollment form for terms and conditions and check eligibility at KaryForward.com/hcp

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/hcp

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. Please see full Prescribing Information.

References: 1. XPOVIO (selinexor) [prescribing information], Newton, MA: Karyopharm Therapeutics Inc.; April 2021. **2.** National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma V.7.2021. Accessed May 6, 2021. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** Gavriatopoulou M, Chari A, Chen C, et al. Integrated safety profile of selinexor in multiple myeloma: experience from 437 patients enrolled in clinical trials. *Leukemia.* 2020;34(9):2430-2440. **4.** Data on File. Karyopharm Therapeutics Inc. 2021. **5.** Mikhael J, Noonan KR, Faiman B, et al. Consensus recommendations for the clinical management of patients with multiple myeloma treated with selinexor. *Clin Lymphoma, Myeloma & Leuk.* 2020;20(6):351-357. **6.** EMEND (aprepitant) [prescribing information]. Whitehouse Station, NJ: Merck & Co, Inc; 2021. **7.** VARUBI (rolapitant) [prescribing information]. Deerfield, IL: TerSera Therapeutics LLC; 2020. **8.** AKYNZEO (netupitant and palonosetron) [prescribing information]. Lugano, Switzerland: Helsinn Healthcare SA; 2020. **9.** Magen H, Geva M, Volchik Y, Avigdor A, Nagler A. Selinexor, bortezomib, and dexamethasone for heavily pretreated multiple myeloma: a case series. *Clin Lymphoma Myeloma Leuk.* 2020;20(12):e947-e955. **10.** National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue V.1.2021. Accessed May 6, 2021. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Karyopharm® Therapeutics