XPOVIO®
(selinexor)

Dosing and Dosage Modification Guide XPOVIO + dexamethasone (Xd) for RRMM

Three key steps to starting your patients on XPOVIO[1]

1. Set expectations

- Counsel patients on what to expect when receiving treatment with XPOVIO + dexamethasone
- Advise patients to maintain adequate fluid and caloric intake throughout treatment

2. Prescribe XPOVIO

- XPOVIO is taken orally on Days 1 and 3 of each week in combination with dexamethasone
- During therapy with XPOVIO, refer to instructions for antiemetics on page 4

3. Monitor your patient

- During therapy with XPOVIO, provide additional antiemetics as needed
- Monitor CBC with differential, standard blood chemistries, body weight, nutritional status, and volume status at baseline and during treatment, more frequently during the first 3 months of treatment
- Consider intravenous hydration for patients at risk of dehydration
- Assess the need for dose modifications (see table below)

Recommended dosage and dose reduction steps for ARs[1]

	DAY 1	DAY 3	TOTAL WEEKLY DOSE
Recommended dosage	80 mg + dexamethasone† 20 mg	80 mg + dexamethasone† 20 mg	160 mg + dexamethasone† 40 mg

DOSE REDUCTION		
First reduction	100 mg	100 mg
Second reduction	80 mg	80 mg
Third reduction	60 mg	60 mg
PERMANENTLY DISCONTINUE		

†For additional information regarding the administration of dexamethasone, refer to the prescribing information.
AR=adverse reaction, CBC=complete blood count, RRMM=relapsed or refractory multiple myeloma.

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.

Please see full Prescribing Information.

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Thrombocytopenia[1]

PROPHYLAXIS

- Monitor platelet counts at baseline and throughout treatment
- Monitor more frequently during the first 3 months of treatment
- Monitor for signs and symptoms of bleeding and evaluate promptly

MANAGEMENT

- Institute platelet transfusion and/or other treatments as clinically indicated
- Interrupt, reduce dose, or permanently discontinue based on severity of the adverse reaction

Dosage modification guidelines

Adverse reaction	Actions (any occurrence)
Platelet count 25,000 to <75,000/mcL	• Reduce XPOVIO® (selinexor) by 1 dose level
Platelet count 25,000 to <75,000/mcL *with* concurrent bleeding	• Interrupt XPOVIO • Restart XPOVIO at 1 dose level lower, after bleeding has resolved • Administer platelet transfusions per clinical guidelines
Platelet count <25,000/mcL	• Interrupt XPOVIO • Monitor until platelet count returns to at least 50,000/mcL • Restart XPOVIO at 1 dose level lower

Weight Loss and Anorexia[1]

PROPHYLAXIS

- Monitor weight, nutritional status, and volume status at baseline and throughout treatment
- Monitor more frequently during the first 3 months of treatment

MANAGEMENT

- Interrupt, reduce dose, or permanently discontinue based on severity of the adverse reaction
- Provide nutritional support, fluids, and electrolyte repletion as clinically indicated

Dosage modification guidelines

Adverse reaction	Actions (any occurrence)
Weight loss of 10% to <20% *OR* anorexia associated with significant weight loss or malnutrition	• Interrupt XPOVIO and institute supportive care • Monitor until weight returns to >90% of baseline weight • Restart XPOVIO at 1 dose level lower

Please see full Prescribing Information.

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Neutropenia[1]

PROPHYLAXIS

- Obtain white blood cell counts with differential at baseline and throughout treatment
- Monitor more frequently during the first 3 months of treatment
- Monitor for signs and symptoms of concomitant infection and evaluate promptly

MANAGEMENT

- Consider supportive measures including antimicrobials and growth factors (e.g., G-CSF)
- Interrupt, reduce dose, or permanently discontinue based on severity of the adverse reaction

Dosage modification guidelines

Adverse reaction	Actions (any occurrence)
Absolute neutrophil count of 0.5 to 1 x 10^9/L without fever	• Reduce XPOVIO® (selinexor) by 1 dose level
Absolute neutrophil count of <0.5 x 10^9/L *OR* febrile neutropenia	• Interrupt XPOVIO • Monitor until neutrophil counts return to 1 x 10^9/L or higher • Restart XPOVIO at 1 dose level lower

Diarrhea[1]

PROPHYLAXIS

- Administer intravenous fluids to prevent dehydration in patients at risk

MANAGEMENT

- Interrupt, reduce dose, or permanently discontinue based on severity of the adverse reaction
- Provide standard anti-diarrheal agents indicated for the control and symptomatic relief of acute nonspecific diarrhea such as:
  - Loperamide, bismuth subsalicylate, or equivalent*
  - Replace electrolytes as clinically indicated

*Please see prescribing information for dosage and administration of agents listed.

Dosage modification guidelines

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

Please see full Prescribing Information.

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Anemia[1]

PROPHYLAXIS

- Monitor hemoglobin

MANAGEMENT

- Administer blood transfusions and/or other treatments per clinical guidelines
- Manage by dose modifications

Dosage modification guidelines

Adverse reaction	Actions (any occurrence)
Hemoglobin <8 g/dL	• Reduce XPOVIO® (selinexor) by 1 dose level • Administer blood transfusions per clinical guidelines
Life-threatening consequences (urgent intervention indicated)	• Interrupt XPOVIO • Monitor hemoglobin until levels return to ≥8 g/dL • Restart XPOVIO at 1 dose level lower • Administer blood transfusions per clinical guidelines

Nausea and Vomiting[1]

PROPHYLACTIC DOUBLE ANTI-NAUSEA COVERAGE

- Ondansetron 8 mg PO[2] 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[3] **OR**
  - Aprepitant 125 mg PO QAM day 1 and 80 mg for 2 days each week[2,4,5]* **OR**
  - Rolapitant 180 mg PO 2 hours before XPOVIO Q2W[2,6]
- Alternatively, once weekly oral dose of Akynzeo (netupitant 300 mg + palonosetron 0.5 mg)[7,8]
- One or both antiemetics may be tapered after 8 weeks of therapy[2]

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

MANAGEMENT

- Interrupt, reduce dose, or permanently discontinue based on severity of the adverse reaction
- Administer intravenous fluids to prevent dehydration and replace electrolytes as clinically indicated

Dosage modification guidelines

Adverse reaction	Actions (any occurrence)
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)	• Maintain XPOVIO and initiate additional anti-nausea medications
Grade 3 nausea (inadequate oral caloric or fluid intake) *OR* Grade ≥3 vomiting (≥6 episodes per day)	• Interrupt XPOVIO • Monitor until nausea or vomiting has resolved to Grade ≤2 or baseline • Initiate additional anti-nausea medications • Restart XPOVIO at 1 dose level lower

Please see full Prescribing Information.

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Fatigue[1]

Dosage modification guidelines	
Adverse reaction	**Actions (any occurrence)**
Grade 2 lasting >7 days or Grade 3	• Interrupt XPOVIO® (selinexor) • Monitor until fatigue resolves to Grade 1 or baseline • Restart XPOVIO at 1 dose level lower

Neurological Toxicity[1]

MANAGEMENT

- 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 the following to avoid exacerbating dizziness or mental status changes:
  - Hydration status
  - Hemoglobin level
  - Concomitant medications
- Institute fall precautions as appropriate
- Manage by dose modifications

Dosage modification guidelines	
Adverse reaction	**Actions (any occurrence)**
Other non-hematologic ARs Grade 3 or 4	• Interrupt XPOVIO • Monitor until resolved to Grade <2; restart XPOVIO at 1 dose level lower

Ocular Toxicity[1]

MANAGEMENT

- Manage with dose modifications and supportive care

Dosage modification guidelines	
Adverse reaction	**Actions (any occurrence)**
Grade 2, excluding cataract	• 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	• Permanently discontinue XPOVIO • Perform ophthalmologic evaluation
Cataract (Grade ≥2)	• Perform ophthalmologic evaluation • Reduce XPOVIO by 1 dose level • Monitor for progression • Hold XPOVIO dose 24 hours prior to surgery and for 72 hours after surgery

Please see full Prescribing Information.

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Hyponatremia[1]

PROPHYLAXIS

- Monitor sodium level at baseline and throughout treatment
- Monitor more frequently during the first 2 months of treatment

MANAGEMENT

- Correct sodium levels for:
  - Concurrent hyperglycemia (serum glucose >150 mg/dL)
  - 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

Dosage modification guidelines

Adverse reaction	Actions (any occurrence)
Sodium level ≤130 mmol/L	• Interrupt XPOVIO® (selinexor), evaluate, and provide supportive care • Monitor until sodium levels return to >130 mmol/L • Restart XPOVIO at 1 dose level lower

SELECTED SAFETY INFORMATION

The most common Grade >3 adverse reactions (incidence ≥20%) were thrombocytopenia, anemia, fatigue, hyponatremia, and neutropenia.

The most common adverse reactions (ARs) (incidence ≥20%) were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The treatment discontinuation rate due to ARs was 27%; 53% of patients had a reduction in the XPOVIO dose, and 65% had the dose of XPOVIO interrupted. The most frequent ARs requiring permanent discontinuation in ≥4% of patients included fatigue, nausea, and thrombocytopenia. Fatal ARs occurred in 9% of patients and serious ARs occurred in 58% of patients.

The approval of XPOVIO + dexamethasone was based upon the efficacy and safety in a prespecified subgroup analysis of the 83 adult patients whose disease was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab, as the benefit-risk ratio appeared to be greater in this more heavily pretreated population than in the overall trial population (N=122).

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. **2.** 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. **3.** Data on File. Karyopharm Therapeutics Inc. 2021. **4.** 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. **5.** EMEND (aprepitant) [prescribing information]. Whitehouse Station, NJ: Merck & Co, Inc. **6.** VARUBI (rolapitant) [prescribing information]. Deerfield, IL: TerSera Therapeutics LLC. **7.** AKYNZEO (netupitant and palonosetron) [prescribing information]. Lugano, Switzerland: Helsinn Healthcare SA. **8.** 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.

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