XPOVIO® (selinexor) 20 mg tablet

Getting patients started on XPOVIO® (selinexor) 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
- Administer a 5-HT3 receptor antagonist, such as ondansetron, and other anti-nausea agents, such as olanzapine or rolapitant, prior to and during treatment*
  - The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommends olanzapine for the prevention of nausea and vomiting*

3. Monitor your patient

- 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)

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

Recommended dosage reduction steps for adverse reactions[1]

	DAY 1	DAY 3	TOTAL WEEKLY DOSE
Recommended dosage	K20 K20 K20 K20 80 mg + dexamethasone† 20 mg	K20 K20 K20 K20 80 mg + dexamethasone† 20 mg	**160 mg** + dexamethasone† 40 mg

DOSE REDUCTION		
First reduction	K20 K20 K20 K20 K20 100 mg	**100 mg**
Second reduction	K20 K20 K20 K20 80 mg	**80 mg**
Third reduction	K20 K20 K20 60 mg	**60 mg**
PERMANENTLY DISCONTINUE		

K20 = 20 mg

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

INDICATION

XPOVIO® (selinexor) in combination with dexamethasone is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies and whose disease is refractory to at least 2 proteasome inhibitors, at least 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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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

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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

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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]

PROPHYLAXIS

- Provide prophylactic antiemetics. Administer 5-HT3 receptor antagonists and other anti-nausea agents prior to and during treatment with XPOVIO
  - The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend olanzapine for the prevention of nausea and vomiting[2]
  - In the STORM clinical trial, 8 mg of ondansetron was required for antiemetic prophylaxis[3,4]
    - Other antiemetics included olanzapine and neurokinin-1 receptor antagonists[3,4]
  - 5-HT3 receptor antagonists indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapies include[2]*:
    - Ondansetron, dolasetron, granisetron, or equivalent for emesis
  - Other anti-nausea medications clinically indicated per the NCCN Guidelines® in combination with other antiemetic agents for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapies include[2]*:
    - Rolapitant tablets, aprepitant for injection, fosaprepitant for injection, or equivalent for emesis

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

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

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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

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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) [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; June 2020. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Antiemesis, V1.2020. © 2020 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed April 2, 2020. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. 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. Published online ahead of print, February 24, 2020. *Leukemia*. doi: 10.1038/s41375-020-0756-6. **4.** Mikhael J, Noonan KR, Faiman B, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(6):351-357.

Karyopharm® Therapeutics