XPOVIO®
(selinexor)

Getting patients started on XPOVIO® (selinexor) for RR DLBCL

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

1. Set expectations

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

2. Prescribe XPOVIO

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

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 and dose modifications for RR DLBCL[1]

	DAY 1	DAY 3	TOTAL WEEKLY DOSE
Recommended dosage	60 mg	60 mg	120 mg
DOSAGE REDUCTION			
First reduction	40 mg	40 mg	80 mg
Second reduction	60 mg		60 mg
Third reduction	40 mg		40 mg
Fourth reduction	PERMANENTLY DISCONTINUE		

CBC=complete blood count, RR DLBCL=relapsed or refractory diffuse large B-cell lymphoma.

INDICATION

XPOVIO (selinexor) is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.

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).

Please see full Prescribing Information.

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
Platelet count 50,000 to <75,000/mcL	**Any occurrence:** • Interrupt 1 dose of XPOVIO® (selinexor) • Restart XPOVIO at the same dose level
Platelet count 25,000 to <50,000/mcL *without* bleeding	**At 1st occurrence:** • Interrupt XPOVIO • Monitor until platelet count returns to at least 50,000/mcL • Reduce XPOVIO by 1 dose level
Platelet count 25,000 to <50,000/mcL *with* concurrent bleeding	**Any occurrence:** • Interrupt XPOVIO • Monitor until platelet count returns to at least 50,000/mcL • Restart XPOVIO at 1 dose level lower, after bleeding has resolved • Administer platelet transfusions per clinical guidelines
Platelet count <25,000/mcL	**Any occurrence:** • Interrupt XPOVIO • Monitor until platelet count returns to at least 50,000/mcL • Restart XPOVIO at 1 dose level lower • Administer platelet transfusions per clinical guidelines

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 more than 90% of baseline weight • Restart XPOVIO at 1 dose level lower

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
Absolute neutrophil count of 0.5 to <1 x 10^9/L without fever	**At 1st occurrence:** • Interrupt XPOVIO • Monitor until neutrophil counts return to 1 x 10^9/L or higher • Restart XPOVIO at the same dose level **At recurrence:** • Interrupt XPOVIO • Monitor until neutrophil counts return to 1 x 10^9/L or higher • Administer growth factors per clinical guidelines • Restart XPOVIO at 1 dose level lower
Absolute neutrophil count <0.5 x 10^9/L *OR* febrile neutropenia	**Any occurrence:** • Interrupt XPOVIO • Monitor until neutrophil counts return to 1 x 10^9/L or higher • Administer growth factors per clinical guidelines • Restart XPOVIO at 1 dose level lower

Diarrhea[1]

PROPHYLAXIS

- Administer intravenous fluids to prevent dehydration

MANAGEMENT

- Interrupt, reduce dose, or permanently discontinue based on severity of the adverse reaction
- Provide standard antidiarrheal 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

Anemia[1]

PROPHYLAXIS
- Monitor hemoglobin

MANAGEMENT
- Administer blood transfusions per clinical guidelines
- Manage by dose modifications

Dosage modification guidelines

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

Nausea and Vomiting

PROPHYLAXIS
- Provide prophylactic antiemetics. Administer 5-HT3 receptor antagonists and other antinausea agents prior to and during treatment with XPOVIO[1]
  - 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]

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 antinausea medications
Grade 3 nausea (inadequate oral caloric or fluid intake) *OR* Grade 3 or higher vomiting (≥6 episodes per day)	• 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

Fatigue[1]

MANAGEMENT

- Manage by dose modifications

Dosage modification guidelines

Adverse reaction	Actions (any occurrence)
Grade 2 lasting >7 days *OR* Grade 3	• Interrupt XPOVIO • 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 or lower; 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, excluding cataract	• Permanently discontinue XPOVIO • Perform ophthalmologic evaluation

XPOVIO® (selinexor)

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, 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 adverse reactions, excluding laboratory abnormalities, in ≥20% of patients were fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities in ≥15% of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in ≥5% were thrombocytopenia (18%), lymphopenia (5%), and neutropenia (9%).

Adverse reactions led to XPOVIO dose interruption in 61% of patients and dose reduction in 49%, with 17% of all patients having 2 or more dose reductions. Discontinuation due to adverse reactions occurred in 17% of patients who received XPOVIO. Fatal adverse reactions occurred in 3.7% of patients within 30 days and 5% of patients within 60 days of last treatment. Serious adverse reactions occurred in 46% of patients who received XPOVIO.

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.; April 2021. **2.** Gavriatopoulou M et al. *Leukemia*. 2020;34(9):2430-2440. **3.** Data on file. Karyopharm Therapeutics Inc. 2021. **4.** Mikhael J et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(6):351-357. **5.** EMEND (aprepitant) [prescribing information]. Whitehouse Station, NJ: Merck & Co, Inc; 2021. **6.** VARUBI (rolapitant) [prescribing information]. Deerfield, IL: TerSera Therapeutics LLC; 2020. **7.** AKYNZEO (netupitant and palonosetron) [prescribing information]. Lugano, Switzerland: Helsinn Healthcare SA; 2020. **8.** Magen H et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(12):e947-e955.

Karyopharm® Therapeutics