XPOVIO® (selinexor) 20 mg tablet

# Relapsed or refractory diffuse large B-cell lymphoma (RR DLBCL) Treatment Protocol Assessment

| | |
|---|---|
| **Patient/MRN:** | **Date:** |
| **Medication/Dose:** | **Week #:** |

## GENERAL INFORMATION

- ☐ Confirm patient name, address, phone number
- ☐ Discuss any changes in health status
- ☐ Verify additional support (caregiver, therapist, etc)

## DISEASE CHARACTERISTICS

Disease type
- ☐ *De novo* DLBCL
- ☐ Transformed DLBCL
- ☐ Unknown

DLBCL histology
- ☐ GCB
- ☐ Non-GCB
- ☐ Unknown

Subtypes
- ☐ Double expressor
- ☐ Triple expressor
- ☐ Double hit
- ☐ Triple hit

Previous stem cell transplant: ☐ Yes, date: ☐ No

Prior treatment(s):

Response to prior treatment(s):

## RECOMMENDED DOSAGE: 60 MG TWICE PER WEEK

| DAY 1 | DAY 2 | DAY 3 | DAY 4 | DAY 5 | DAY 6 | DAY 7 |
|---|---|---|---|---|---|---|
| **XPOVIO 60 mg** K20 K20 K20 20 mg tablet x 3 | | **XPOVIO 60 mg** K20 K20 K20 20 mg tablet x 3 | | | | |

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## PATIENT ASSESSMENT FOR ADVERSE REACTIONS (ARs)

Discuss any ARs the patient is experiencing, including:

- ☐ Signs/symptoms of bleeding and easy bruising
- ☐ Signs/symptoms of infection
- ☐ Nausea/vomiting
- ☐ Diarrhea
- ☐ Fatigue
- ☐ Shortness of breath
- ☐ Decreased appetite or weight loss
- ☐ Neurological toxicity (dizziness, confusion)
- ☐ Blurred vision

- ☐ Review symptoms that should trigger a call to the healthcare team or ER
- ☐ Verify labs are being done as clinically indicated, more frequently during the first 3 months of treatment

Review lab results for indications of ARs, including:

- ☐ Thrombocytopenia
- ☐ Neutropenia
- ☐ Anorexia/weight loss
- ☐ Hyponatremia
- ☐ Neurological toxicity
- ☐ Other laboratory abnormalities:

- ☐ Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment and for 1 week after the final dose
- ☐ Advise patients to refrain from driving and engaging in hazardous occupations or activities if they are experiencing neurological toxicity

## SUPPORTIVE CARE

- ☐ Verify patient has supportive care medications and understands proper administration
  - Ensure prescription for a 5-HT3 receptor antagonist and other anti-nausea agents
- ☐ Remind patient to maintain adequate fluid and caloric intake throughout treatment

### Thrombocytopenia

- ☐ Platelet transfusion and/or other treatments

### Nausea/vomiting

- ☐ 5-HT3 receptor antagonists
- ☐ Other anti-nausea agents
- ☐ Intravenous fluids and electrolytes to prevent dehydration

### Dehydration

- ☐ Intravenous hydration and electrolyte replacement

### Diarrhea

- ☐ Anti-diarrheal agents

### Anorexia/weight loss

- ☐ Nutritional support
- ☐ Fluids
- ☐ Electrolyte repletion

### Neutropenia

- ☐ Antimicrobials
- ☐ Growth factors (e.g., G-CSF)

### Hyponatremia

- ☐ Intravenous saline, as appropriate
- ☐ Salt tablets, as appropriate
- ☐ Dietary review

### Neurological toxicity

- ☐ Optimize hydration status
- ☐ Optimize hemoglobin level
- ☐ Prescribe concomitant medications
- ☐ Institute fall precautions

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## MANAGEMENT OF HEMATOLOGIC ARs WITH XPOVIO FOR RR DLBCL

### Thrombocytopenia

- Platelet count 50,000 to <75,000/mcL
  - ☐ Interrupt 1 dose
  - ☐ Restart at same dose level
- Platelet count 25,000 to <50,000/mcL *without* bleeding, first occurrence
  - ☐ Interrupt dosing
  - ☐ Monitor until platelet count returns to at least 50,000/mcL
  - ☐ Reduce dose by 1 level
- Platelet count 25,000 to <50,000/mcL *with* concurrent bleeding
  - ☐ Interrupt dosing
  - ☐ Monitor until platelet count returns to at least 50,000/mcL
  - ☐ Restart at 1 dose level lower, after bleeding has resolved
  - ☐ Platelet transfusions per clinical guidelines
- Platelet count <25,000/mcL
  - ☐ Interrupt dosing
  - ☐ Monitor until platelet count returns to at least 50,000/mcL
  - ☐ Restart at 1 dose level lower
  - ☐ Platelet transfusions per clinical guidelines

### Neutropenia

- Absolute neutrophil count of 0.5 to <1 x $10^9$/L without fever, first occurrence
  - ☐ Interrupt dosing
  - ☐ Monitor until neutrophil counts return to ≥1 x $10^9$/L
  - ☐ Restart at same dose level
- Absolute neutrophil count of 0.5 to <1 x $10^9$/L without fever, recurrence
  - ☐ Interrupt dosing
  - ☐ Monitor until neutrophil counts return to ≥1 x $10^9$/L
  - ☐ Administer growth factors per clinical guidelines
  - ☐ Restart at 1 dose level lower
- Absolute neutrophil count of <0.5 x $10^9$/L *OR* febrile neutropenia
  - ☐ Interrupt dosing
  - ☐ Monitor until neutrophil counts return to ≥1 x $10^9$/L
  - ☐ Growth factors per clinical guidelines
  - ☐ Restart at 1 dose level lower

### Anemia

- Hemoglobin <8 g/dL
  - ☐ Reduce 1 dose level
  - ☐ Blood transfusions per clinical guidelines
- Life-threatening consequences
  - ☐ Interrupt dosing
  - ☐ Monitor until hemoglobin levels return to ≥8 g/dL
  - ☐ Restart at 1 dose level lower
  - ☐ Blood transfusions per clinical guidelines

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## MANAGEMENT OF NON-HEMATOLOGIC ARs WITH XPOVIO FOR RR DLBCL

### 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 of vomiting per day)
  - ☐ Maintain dosing
  - ☐ Initiate additional anti-nausea medications
- Grade 3 nausea (inadequate oral caloric or fluid intake *OR* ≥6 episodes of vomiting per day)
  - ☐ Interrupt dosing
  - ☐ Monitor until nausea or vomiting has resolved to Grade ≤2 or baseline
  - ☐ Initiate additional anti-nausea medications
  - ☐ Restart at 1 dose level lower

### Diarrhea

- Grade 2 (increase of 4 to 6 stools per day over baseline), first occurrence
  - ☐ Maintain dosing
  - ☐ Institute supportive care
- Grade 2 (increase of 4 to 6 stools per day over baseline), second and subsequent occurrences
  - ☐ Reduce by 1 dose level
  - ☐ Institute supportive care
- Grade ≥3 (increase of ≥7 stools per day over baseline; hospitalization indicated)
  - ☐ Interrupt dosing
  - ☐ Institute supportive care
  - ☐ Monitor until diarrhea resolves to Grade ≤2
  - ☐ Restart at 1 dose level lower

### Weight loss and anorexia

- Weight loss of 10% to <20% *OR* anorexia associated with significant weight loss or malnutrition
  - ☐ Interrupt dosing
  - ☐ Institute supportive care
  - ☐ Monitor until weight returns to >90% of baseline weight
  - ☐ Restart at 1 dose level lower

### Hyponatremia

- Sodium: ≤130 mmol/L
  - ☐ Interrupt dosing
  - ☐ Evaluate and provide supportive care
  - ☐ Monitor until levels return to >130 mmol/L
  - ☐ Restart at 1 dose level lower

### Fatigue

- Grade 2 lasting >7 days *OR* Grade 3
  - ☐ Interrupt dosing
  - ☐ Monitor until fatigue resolves to Grade 1 or baseline
  - ☐ Restart at 1 dose level lower

### Other non-hematologic ARs

- Grade 3 or 4
  - ☐ Interrupt dosing
  - ☐ Monitor until resolved to Grade ≤2
  - ☐ Restart at 1 dose level lower

### Ocular toxicity

- Grade 2, excluding cataract
  - ☐ Perform ophthalmologic evaluation
  - ☐ Interrupt XPOVIO and provide supportive care
  - ☐ Monitor until ocular symptoms resolve to Grade 1 or baseline
  - ☐ Restart at 1 dose level lower
- Grade ≥3
  - ☐ Permanently discontinue
  - ☐ Perform ophthalmologic evaluation
- Cataract (Grade ≥2)
  - ☐ Perform ophthalmologic evaluation
  - ☐ Reduce by 1 dose level
  - ☐ Monitor for progression
  - ☐ Hold dose for 24 hours prior to surgery and for 72 hours after surgery

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## DOSING REVIEW: RECOMMENDED DOSAGE - 60 MG TWICE PER WEEK

Verify change in XPOVIO dosing and schedule, if appropriate

- ☐ 1st reduction: 40 mg twice per week
- ☐ 2nd reduction: 60 mg once per week
- ☐ 3rd reduction: 40 mg once per week
- ☐ 4th reduction: Permanently discontinue

## MEDICATION REVIEW

Current medications, prescription and non-prescription:

- ☐ Review change in dosing and schedule, if appropriate
- ☐ Reinforce patient education as needed

## ADHERENCE

Assess patient adherence

- Number of doses missed (per week/per month):
- Reason for missed dose:

Address any issues with nonadherence

- Action taken to resolve adherence issues:

## MONITORING AND FOLLOW-UP

- ☐ Verify follow-up call, healthcare appointments, lab testing appointments
- ☐ Review medication refill process
- ☐ Verify labs are being done as clinically indicated, more frequently during the first 3 months of treatment
- ☐ Ask the patient if they have any additional questions:

**The treatment assessment protocol outlined within has been developed from the FDA-approved US Prescribing Information for XPOVIO® (selinexor). The aim of the treatment assessment protocol is to help clinicians to make informed decisions about their patients who are prescribed XPOVIO. Adherence to this protocol does not guarantee a successful outcome. Healthcare professionals must make their own treatment decisions about care, and this treatment assessment protocol is not intended to take the place of physician judgment in treatment of patients who use XPOVIO.**

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## 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).

## IMPORTANT SAFETY INFORMATION

**Thrombocytopenia:** XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia is the leading cause of dose modifications.

Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Institute platelet transfusion and/or other treatments as clinically indicated. Monitor patients for signs and symptoms of bleeding and evaluate promptly. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction (AR).

**Neutropenia:** XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection.

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 ARs.

**Gastrointestinal Toxicity:** XPOVIO can cause severe gastrointestinal toxicities.

**Nausea/Vomiting:** Provide prophylactic antiemetics. Administer 5-HT3 receptor antagonists and other anti-nausea agents prior to and during treatment with XPOVIO. Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Administer intravenous fluids to prevent dehydration and replace electrolytes as clinically indicated.

**Diarrhea:** Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Provide standard anti-diarrheal agents, administer intravenous fluids to prevent dehydration, and replace electrolytes as clinically indicated.

**Anorexia/Weight Loss:** 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 ARs. Provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

**Hyponatremia:** XPOVIO can cause severe or life-threatening hyponatremia.

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 ARs.

**Serious Infection:** XPOVIO can cause serious and fatal infections. Most of these infections were not associated with Grade 3 or higher neutropenia. Atypical infections reported after XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Monitor for signs and symptoms of infection and evaluate and treat promptly.

## IMPORTANT SAFETY INFORMATION (cont'd)

**Neurological Toxicity:** XPOVIO® (selinexor) 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, 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.

**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.

## ADVERSE REACTIONS

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

Fatal ARs occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal AR was infection. Serious ARs occurred in 46% of patients who received XPOVIO; the most frequent serious AR was infection.

Discontinuation due to ARs occurred in 17% of patients who received XPOVIO. ARs resulting in discontinuation in ≥2% of patients included: infection, fatigue, thrombocytopenia, and nausea.

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.

## USE IN SPECIFIC POPULATIONS

Clinical studies of XPOVIO in patients with relapsed or refractory DLBCL did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

The effect of end-stage renal disease ($CL_{CR}$<15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

**Please see 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.**