XPOVIO® (selinexor)

Treatment Protocol Assessment

for patients with multiple myeloma (MM) who have received at least one prior therapy

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)

Age: .....

Sex: .....

Time since initial diagnosis (months): .....

DISEASE CHARACTERISTICS

Baseline ECOG performance status
- ☐ 0
- ☐ 1
- ☐ 2

R-ISS score
- ☐ I
- ☐ II
- ☐ III
- ☐ Unknown

Creatinine clearance, mL/min
- ☐ <30
- ☐ 30–59
- ☐ ≥60

High-risk cytogenetics
- ☐ del(17p)/p53
- ☐ t(14;16)
- ☐ t(4;14)
- ☐ 1q21
- ☐ Not assessed

Other gene mutations
- ☐ del(13)
- ☐ t(6;14)
- ☐ t(11;14)
- ☐ t(14;20)

Plasma cells at initial diagnosis
- ☐ <50
- ☐ ≥50

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

Prior treatment(s): .....

.....

Response to prior treatment(s): .....

.....

Weeks since end of prior therapy: .....

.....

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 treating their patients who are prescribed XPOVIO. You may refer to the full prescribing information for more detailed information. 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 prescribed XPOVIO.

Please see Important Safety Information on pages 7 and 8.

XPOVIO® (selinexor) MM
TREATMENT PROTOCOL ASSESSMENT

Patient/MRN:	Date:
Medication/Dose:	Week #:

RECOMMENDED DOSAGE FOR XPOVIO + Vd REGIMEN: 100 mg ONCE WEEKLY

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

 = 50 mg

Prescribed dosing:

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7

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, of the potential risk to a fetus and use of effective contraception

☐ Advise patients not to drive or engage in hazardous occupations or activities if they are experiencing neurological toxicity

Patient/MRN:	Date:
Medication/Dose:	Week #:

SUPPORTIVE CARE

- [ ] Verify patient has supportive care medications and understands proper administration
- [ ] Remind patient to maintain adequate fluid and caloric intake throughout treatment

Thrombocytopenia

- [ ] Platelet transfusion and/or other treatments

Nausea and vomiting (potential antiemetics to consider prophylactically)

- [ ] 5-HT3 antagonist (ondansetron 8 mg, or equivalent)*
- [ ] Other: olanzapine 2.5-5 mg
- [ ] Other: NK1R antagonist, e.g., aprepitant (80-125 mg) or rolapitant (180 mg)*
- [ ] Other: netupitant (300 mg) + palonosetron (0.5 mg)*†

Dehydration

- [ ] Intravenous hydration and electrolyte replacement

Diarrhea

- [ ] Antidiarrheal 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

*Refer to individual drug package inserts for dosing schedules.
†Netupitant + palonosetron is a combination of an NK1R antagonist and a 5-HT3 antagonist, respectively.

MANAGEMENT OF HEMATOLOGIC ARs

Thrombocytopenia

Platelet count 25,000 to <75,000/mcL

- ☐ Reduce by 1 dose level

Platelet count 25,000 to <75,000/mcL *with* concurrent bleeding

- ☐ Interrupt dosing
- ☐ Restart at 1 dose level lower after bleeding has resolved
- ☐ Administer platelet transfusions per clinical guidelines

Platelet count <25,000/mcL

- ☐ Interrupt dosing
- ☐ Monitor until platelet count returns to ≥50,000/mcL
- ☐ Restart at 1 dose level lower

Neutropenia

Absolute neutrophil count of 0.5 to 1 x 10^9/L without fever

- ☐ Reduce by 1 dose level

Absolute neutrophil count <0.5 x 10^9/L *OR* febrile neutropenia

- ☐ Interrupt dosing
- ☐ Monitor until neutrophil counts return to ≥1 x 10^9/L
- ☐ Restart at 1 dose level lower

Anemia

Hemoglobin <8 g/dL

- ☐ Reduce by 1 dose level
- ☐ Administer blood transfusions per clinical guidelines

Life-threatening consequences

- ☐ Interrupt dosing
- ☐ Monitor hemoglobin until levels return to ≥8 g/dL
- ☐ Restart at 1 dose level lower
- ☐ Administer blood transfusions per clinical guidelines

Patient/MRN:	Date:
Medication/Dose:	Week #:

MANAGEMENT OF NONHEMATOLOGIC ARs

Nausea and vomiting (during therapy with XPOVIO, provide additional antiemetics as needed)

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 dosing
- ☐ Initiate additional antinausea medication
- ☐ Add olanzapine daily for 1-2 months

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

- ☐ Maintain NK1R antagonist
- ☐ Interrupt XPOVIO dosing until resolved to Grade 2 or lower
- ☐ Monitor until nausea or vomiting has resolved to Grade ≤2 or baseline
- ☐ Restart XPOVIO 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 level ≤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 nonhematologic 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 dosing 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

Please see Important Safety Information on pages 7 and 8.

Patient/MRN:	Date:
Medication/Dose:	Week #:

DOSING REVIEW: RECOMMENDED DOSAGE FOR XPOVIO—100 mg ONCE PER WEEK

Verify change in dosing and schedule, if appropriate

- ☐ 1st reduction: 80 mg once weekly
- ☐ 2nd reduction: 60 mg once weekly
- ☐ 3rd reduction: 40 mg once weekly
- ☐ 4th reduction: Permanently discontinue

MEDICATION REVIEW

Current medications, prescription and nonprescription: .....

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

ADHERENCE

Assess patient adherence

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

Address any issues with nonadherence

- Action taken to resolve adherence issues: .....

MONITORING AND FOLLOWUP

- ☐ 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:

INDICATION

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.

IMPORTANT SAFETY INFORMATION

Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma.

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

Monitor more frequently during the first 3 months of treatment. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients.

Nausea/Vomiting/Diarrhea: Provide prophylactic antiemetics or treatment as needed.

Anorexia/Weight Loss: Monitor weight, nutritional status, and volume status at baseline and throughout treatment and 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.

Serious Infection: XPOVIO can cause serious and fatal infections. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Neurological Toxicity: XPOVIO 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 until the neurological toxicity fully resolves. 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.

Cataracts: New onset or exacerbation of cataract has occurred during treatment with XPOVIO. The incidence of new onset or worsening cataract requiring clinical intervention was reported.

Continued on page 8.

IMPORTANT SAFETY INFORMATION (Continued from page 7)

ADVERSE REACTIONS

The most common adverse reactions (ARs) (≥20%) in patients with multiple myeloma who received XVd 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.

Fatal ARs occurred in 6% of patients within 30 days of last treatment. Serious ARs occurred in 52% of patients. Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, peripheral neuropathy and vomiting. Adverse reactions led to XPOVIO dose interruption in 83% of patients and dose reduction in 64% of patients.

USE IN SPECIFIC POPULATIONS

No overall difference in effectiveness of XPOVIO 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.

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.