Dosing and Dose Modification Guide

Expand your patients' treatment options with XPOVIO®

PrXPOVIO®
selinexor tablets

XPOVIO® is the **first and only XPO1 inhibitor** for multiple myeloma, helping to restore tumour suppressor pathways in the cell's nucleus, leading to cell cycle arrest and apoptosis.

A new class of therapy in multiple myeloma

XPOVIO® (selinexor) is indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Please see the XPOVIO® Product Monograph for complete dosing and administration information. For additional information regarding the administration of bortezomib and dexamethasone, refer to their respective Product Monographs.

Getting patients started on XPOVIO®[1]

Dosing considerations

Advise patients to maintain adequate fluid and caloric intake throughout treatment.

Consider intravenous hydration for patients at risk of dehydration.

Provide prophylactic antiemetics. Administer a 5-HT3 receptor antagonist and other anti-nausea agents prior to and during treatment with XPOVIO®.

Administration

Each XPOVIO® dose should be taken orally at approximately the same time of day.

Each tablet should be swallowed whole with water.

Do not break, chew, crush, or divide the tablets.

XPOVIO® can be taken with or without food.

Missed dose

If an XPOVIO® dose is missed or delayed or a patient vomits after a dose of XPOVIO®, the patient should not repeat the dose. Patients should take the next dose on the next regularly scheduled day.

Once-weekly XPOVIO® dosing

Recommended starting dosage and schedule[1]

DAY 1

XPOVIO® 100 mg
(five 20 mg tablets)
+ bortezomib 1.3 mg/m²
(for 4 weeks followed by 1 week off)
+ dexamethasone 20 mg

DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
dexamethasone 20 mg	**No dose**	**No dose**	**No dose**	**No dose**	**No dose**

- The recommended starting dose of XPOVIO® in combination with bortezomib and dexamethasone in a 35-day cycle is as follows:
  - XPOVIO® 100 mg (five 20 mg tablets) taken orally once weekly on Day 1 of each week.
  - bortezomib 1.3 mg/m² administered subcutaneously once weekly on Day 1 of each week for 4 weeks followed by 1 week off.
  - dexamethasone 20 mg taken orally twice weekly on Days 1 and 2 of each week.

- Treatment is administered until disease progression or unacceptable toxicity.

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XPOVIO® dosage reduction steps[1]

	XPOVIO® IN COMBINATION WITH BORTEZOMIB AND DEXAMETHASONE (XVd)
Recommended starting dosage	100 mg ONCE WEEKLY
First reduction	80 mg ONCE WEEKLY
Second reduction	60 mg ONCE WEEKLY
Third reduction	40 mg ONCE WEEKLY
Fourth reduction*	**PERMANENTLY DISCONTINUE**

* If symptoms do not resolve, treatment should be discontinued.

Monitoring and managing XPOVIO®[1]

Monitoring and laboratory tests

Platelet counts, hemoglobin, and white blood cell count with differential should be monitored at baseline and throughout treatment with XPOVIO®. Consider more frequent monitoring during the first 3 months of treatment.

Sodium level, patient weight, nutritional status, and volume status should be monitored at baseline, throughout treatment and as clinically indicated. Monitor sodium level more frequently during the first 2 months of treatment.

Dosage modification for hematologic adverse reactions

Adverse Reaction	Occurrence	Action
Thrombocytopenia		
Platelet count 25 x 10^9/L to less than 75 x 10^9/L	Any	• Reduce XPOVIO® by 1 dose level.
Platelet count 25 x 10^9/L to less than 75 x 10^9/L with concurrent bleeding	Any	• Interrupt XPOVIO®. • Restart XPOVIO® at 1 dose level lower after bleeding has resolved. • Administer platelet transfusions per clinical guidelines.
Platelet count less than 25 x 10^9/L	Any	• Interrupt XPOVIO®. • Monitor until platelet count returns to at least 50 x 10^9/L. • Restart XPOVIO® at 1 dose level lower.
Neutropenia		
Absolute neutrophil count of 0.5 to 1 x 10^9/L without fever	Any	• Reduce XPOVIO® by 1 dose level.
Absolute neutrophil count less than 0.5 x 10^9/L OR febrile neutropenia	Any	• Interrupt XPOVIO®. • Monitor until neutrophil counts return to 1 x 10^9/L or higher. • Restart XPOVIO® at 1 dose level lower.
Anemia		
Hemoglobin less than 80 g/L	Any	• Reduce XPOVIO® by 1 dose level. • Administer blood transfusions and/or other treatments per clinical guidelines.
Life-threatening consequences	Any	• Interrupt XPOVIO®. • Monitor hemoglobin until levels return to 80 g/L or higher. • Restart XPOVIO® at 1 dose level lower. • Administer blood transfusions and/or other treatments per clinical guidelines.

Dosage modification for non-hematologic adverse reactions

Adverse Reaction	Occurrence	Action
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 or fewer episodes per day)	Any	• Maintain XPOVIO® and initiate additional anti-nausea medications.
Grade 3 nausea (inadequate oral caloric or fluid intake) OR Grade 3 or higher vomiting (6 or more episodes per day)	Any	• Interrupt XPOVIO®. • Monitor until nausea or vomiting has resolved to Grade 2 or lower or baseline. • Initiate additional anti-nausea medications. • Restart XPOVIO® at 1 dose level lower.
Diarrhea		
Grade 2 (increase of 4 to 6 stools per day over baseline)	1st	• Interrupt XPOVIO® and institute supportive care. • Monitor until diarrhea resolves to Grade 1 or lower. • Restart XPOVIO® at current dose.
	2nd and subsequent	• Interrupt XPOVIO® and institute supportive care. • Monitor until diarrhea resolves to Grade 1 or lower. • Restart XPOVIO® at 1 dose level lower.
Grade 3 or higher (increase of 7 stools or more per day over baseline; hospitalization indicated)	Any	• Interrupt XPOVIO® and institute supportive care. • Monitor until diarrhea resolves to Grade 1 or lower. • Restart XPOVIO® at 1 dose level lower.
Weight Loss and Anorexia		
Weight loss of 10% to less than 20% OR Anorexia associated with significant weight loss or malnutrition	Any	• Interrupt XPOVIO® and institute supportive care. • Monitor until weight returns to more than 90% of baseline weight. • Restart XPOVIO® at 1 dose level lower.
Hyponatremia		
Sodium level 130 – 120 mmol/L	Any	• Maintain XPOVIO® dose and provide appropriate supportive care. • Monitor sodium levels.
Sodium level 120 mmol/L or less	Any	• Interrupt XPOVIO®, evaluate, and provide supportive care. • Monitor until sodium levels return to greater than 130 mmol/L. • Restart XPOVIO® at 1 dose level lower.

Dosage modification for non-hematologic adverse reactions

Adverse Reaction	Occurrence	Action
Fatigue		
Grade 2 lasting greater than 7 days OR Grade 3	1st	• Interrupt XPOVIO®. • Monitor until fatigue resolves to Grade 1 or baseline. • Restart XPOVIO® at current dose.
	2nd and subsequent	• Interrupt XPOVIO®. • Monitor until fatigue resolves to Grade 1 or baseline. • Restart XPOVIO® at 1 dose level lower.
Ocular Toxicity*		
Grade 2, excluding cataract	Any	• 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	Any	• Permanently discontinue XPOVIO®. • Perform ophthalmologic evaluation.
Cataract (Grade ≥2)	Any	• 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.

Adverse Reaction	Occurrence	Action
Other Non-Hematologic Adverse Reactions		
Grade 3 or 4	Any	• Interrupt XPOVIO®. • Monitor until resolved to Grade 2 or lower, restart XPOVIO® at 1 dose level lower.

* Ocular toxicities may include blindness, cataracts, visual acuity reduced, vision blurred, and visual impairment.

ForYOU™
Patient Support Program

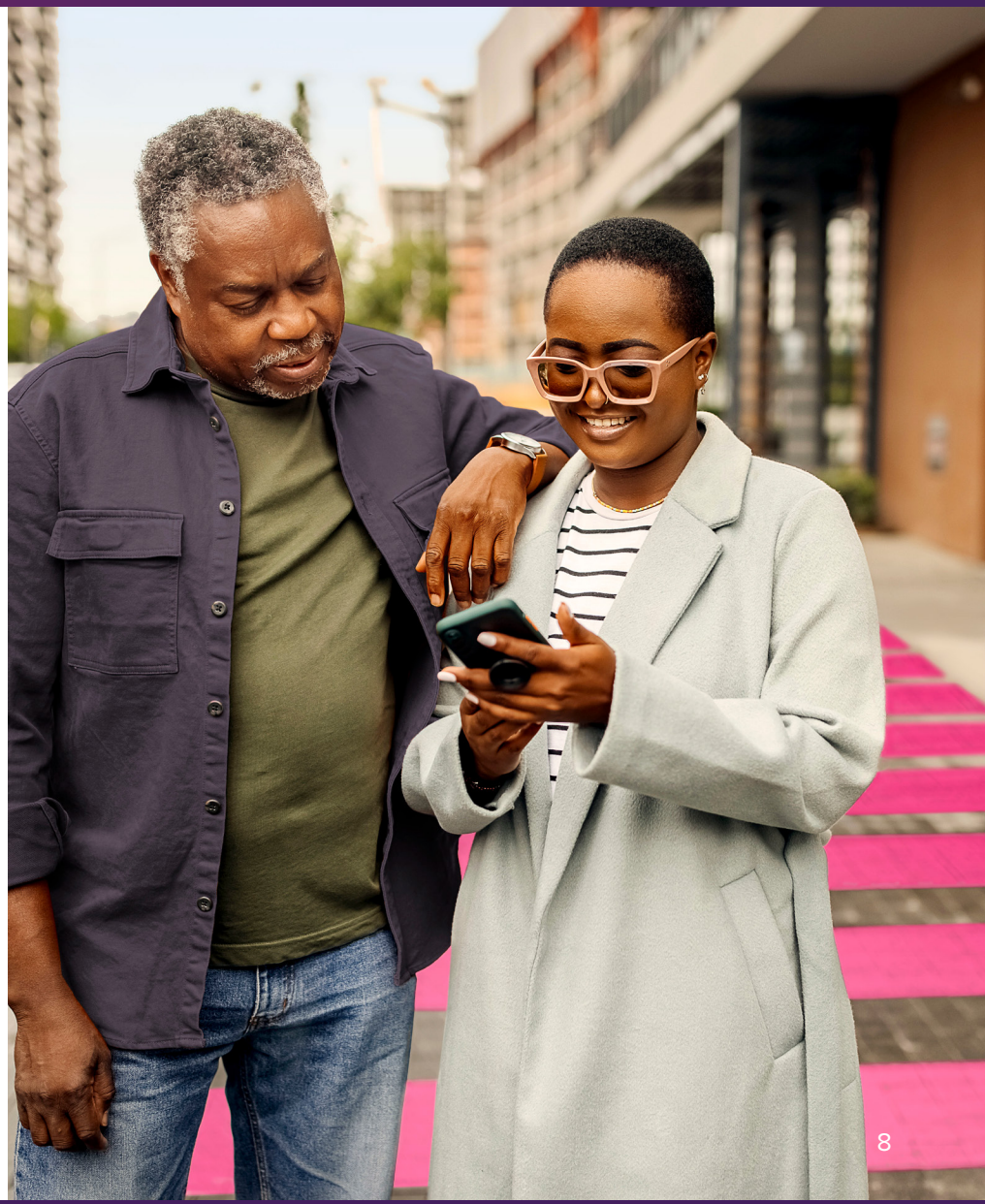
The ForYOU™ Patient Support Program is designed to support XPOVIO® patients and their caregivers throughout the treatment journey.

The program offers:

- **Reimbursement Navigation and Financial Support**
  Support for patients to gain access to XPOVIO®.
- **Treatment Support**
  Education by a dedicated program oncology nurse for patients and their caregivers related to multiple myeloma and treatment with XPOVIO®.

  Ongoing support available throughout treatment with XPOVIO® based on individual patient and caregiver needs.
- **Personalized Solutions**
  Connections for patients and caregivers to third-party resources, providing practical support throughout the XPOVIO® treatment journey.

For inquiries and more information on the ForYOU™ Patient Support Program, please call 1-833-4YOUPSP (1-833-496-8777) between 9AM–5PM ET Monday–Friday, or email xpovio@foryoupsp.com.



Clinical Use:
No overall differences in effectiveness were observed between patients ≥ 65 years of age and younger patients. Older patients had a higher incidence of serious adverse reactions and discontinuation due to an adverse reaction than younger patients.

Relevant Warnings and Precautions:

- Maintenance of adequate fluid and caloric intake.
- Driving and operating machinery.
- Severe or life-threatening hyponatremia.
- Nausea, vomiting, and diarrhea.
- Weight loss and anorexia.
- Life-threatening thrombocytopenia.
- Life-threatening neutropenia.
- Tumour lysis syndrome.
- Serious and fatal infections.
- Monitoring platelet counts, hemoglobin, and white blood cell counts, sodium level, patient weight, nutritional status, and volume status.
- Life-threatening neurologic toxicities.
- New onset or exacerbation of cataract.
- Fertility impairment in females and males of reproductive potential.
- Use of contraception in females of reproductive potential and in males with a female partner of reproductive potential.
- Use in pregnant or breastfeeding women.
- Use in pediatric and geriatric patients.

For More Information:

Please consult the Product Monograph at www.xpoviopm.ca for full prescribing details, including important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling us at 1-866-542-7500.

Reference:

1. FORUS Therapeutics Inc. XPOVIO® (selinexor tablets) Product Monograph. March 22, 2024.

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FORUS THERAPEUTICS