Pr XPOVIO®
selinexor tablets

Feeling well, doing well: Optimizing outcomes through effective patient management

Focus on transient, treatment-related nausea

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.

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.

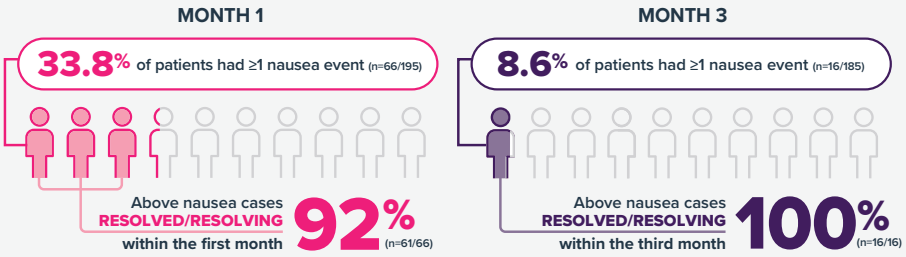
The supportive care guidance provided herein is prepared by FORUS Therapeutics Inc. and should not be relied upon as being complete or mandate any particular course of medical care. It is intended to inform on the incidence of treatment-related nausea and available evidence to date for its management. All treatment decisions are solely at the discretion of the treating physician or healthcare professional.

Treatment-related nausea with XPOVIO® in combination with bortezomib and dexamethasone was generally **transient** and **manageable**[1,2]

In the BOSTON trial, nausea was one of the most frequently observed adverse drug reactions in patients, with most events occurring during the first 8 weeks of treatment. Nausea events were observed in 50% of patients, with Grade 1 or 2 events being the most common (8% Grade 3 or higher).[1]

Nausea events were generally dose and schedule dependent, and were mitigated with prophylactic measures, vigilant monitoring and management, and dose reductions.*[3] The BOSTON trial protocol required a prophylactic 5-HT3 antagonist to address nausea but allowed for other interventions as required.[2]

Nausea associated with XVd was transient and resolved over time[2]



Percentage of patients experiencing **nausea decreased in the first month** of receiving XPOVIO® in combination with bortezomib and dexamethasone using appropriate antiemetic measures.[2]

*XPOVIO® dosing in the BOSTON trial was 100 mg taken orally, once weekly. The median dosage was 80 mg (range 30–137 mg) taken weekly.[1]

Nausea should be managed **proactively** and **early**[1]

XPOVIO® dosage modification for nausea[1]

Grade	Management
Grade 1 or 2 nausea (oral intake decreased without significant weight loss, dehydration, or malnutrition)	• Maintain XPOVIO® and initiate additional anti-nausea medications
Grade 3 nausea (inadequate oral caloric or fluid intake)	• Interrupt XPOVIO® • Monitor until nausea has resolved to Grade 2 or lower or baseline • Initiate additional anti-nausea medications • Restart XPOVIO® at 1 dose level lower*

To report SUSPECTED ADVERSE REACTIONS, contact **FORUS Therapeutics Inc.** at **1-866-542-7500** or **Health Canada** at **1-866-234-2345** or **www.canada.ca/medeffect.**

*In combination with bortezomib and dexamethasone for multiple myeloma, the recommended starting dosage of XPOVIO® is 100 mg once weekly. In the event of adverse reactions, the dose should be reduced to 80 mg once weekly for the first reduction, 60 mg once weekly for the second reduction, and then 40 mg once weekly for the third reduction. If symptoms do not resolve after the third dose reduction, treatment should be permanently discontinued.

Additional recommendations for nausea management from the medical literature

Provide prophylactic antiemetics.[1] Administer a 5-HT3 receptor antagonist and other anti-nausea agents prior to and during treatment with XPOVIO®.[1]

Once-weekly oral dose of Akynzeo®
(netupitant 300 mg + palonosetron 0.5 mg)[8,9]
Given 1 hour prior to dose of XPOVIO®

OR

Ondansetron
8 mg orally 30 to 60 minutes prior to each dose and continued every 8 hours for 2 days following dosing[3,4]

+

Olanzapine
2.5 mg–5.0 mg orally each day at bedtime[3,5]

and/or

Aprepitant*
125 mg orally each morning on Day 1 and 80 mg for 2 days each week[3,6,7]

- One or both antiemetics may be tapered after 6–8 weeks[6]
- Advise patients to maintain adequate fluid and caloric intake[6]

Please see the XPOVIO® Product Monograph for complete dosing and administration information.

For additional information regarding the dosing and administration of bortezomib, dexamethasone, ondansetron, aprepitant, netupitant, and palonosetron, refer to their respective Product Monographs. Olanzapine is not indicated for the treatment of nausea associated with cancer therapy.

*Using dexamethasone together with aprepitant or Akynzeo® may increase the effects of dexamethasone. If using either of these agents, the dose of dexamethasone may need to be reduced.[7,8]

Safety information

In the BOSTON trial, the most frequent treatment-emergent adverse events in >20% of patients receiving XPOVIO® in combination with bortezomib and dexamethasone were thrombocytopenia, nausea, fatigue, anemia, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, weight decreased, asthenia, cataract, and vomiting.

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, 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 of 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 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.

ForYOU™
Patient Support Program

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

For more information, call **1-833-4YOUPSP (1-833-496-8777)** between 9AM–5PM ET Monday–Friday, or email **xpovio@foryoupsp.com**.

References:

1. FORUS Therapeutics Inc. XPOVIO® (selinexor tablets) Product Monograph. March 22, 2024.
2. Data on File. Karyopharm Therapeutics Inc. 2021.
3. Gavriatopoulou M, et al. Integrated safety profile of selinexor in multiple myeloma. *Leukemia*. 2020;34(9):2430-2440.
4. Novartis Pharmaceuticals Canada Inc. ZOFRAN® (ondansetron) Product Monograph. November 9, 2021.
5. Eli Lilly Canada Inc. ZYPREXA® (olanzapine) Product Monograph. January 29, 2020.
6. Mikhael J, et al. Consensus recommendations for the clinical management of patients with multiple myeloma treated with selinexor. *Clin Lymphoma Myeloma Leuk*. 2020;20(6):351-357.
7. Merck Canada Inc. EMEND® (aprepitant) Product Monograph. January 22, 2014.
8. Knight Therapeutics Inc. AKYNZEO® (netupitant and palonosetron) Product Monograph. November 15, 2022.
9. Magen H, et al. Selinexor, bortezomib, and dexamethasone for heavily pretreated multiple myeloma: a case series. *Clin Lymphoma Myeloma Leuk*. 2020;20(12):e947-e955.

Information contained herein based on Data on File refers to proprietary data which has been reviewed and validated by Karyopharm Therapeutics Inc. Data on file has not been independently validated by FORUS Therapeutics Inc.

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