Drug Monograph

Drug Name | Mechanism of Action and Pharmacokinetics | Indications and Status | Adverse Effects | Dosing | Administration Guidelines | Special Precautions | Interactions | Recommended Clinical Monitoring | Supplementary Public Funding | References | Disclaimer

A - Drug Name

selinexor

COMMON TRADE NAME(S): Xpovio®

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B - Mechanism of Action and Pharmacokinetics

Selinexor is a selective inhibitor of nuclear export (SINE) that blocks exportin 1 (XPO1). XPO1 is overexpressed in multiple myeloma cells and is the major mediator of the nuclear export of tumour suppressor proteins (TSPs), growth regulators and mRNAs of growth promoting (oncogenic) proteins. Treatment with selinexor blocks the export of proteins, leading to accumulation of proteins in the nucleus and to inhibition of cell growth, cell cycle arrest, reductions in several oncoproteins, and apoptosis of cancer cells.

Absorption	T max	1.9 h (mean)
	Effects with food	Administration of high-fat or low-fat meal did not appear to have any clinically significant effects on C_{max} and AUC.
Distribution	PPB	95%
	Cross blood brain barrier?	Yes
Metabolism	Selinexor is metabolized by CYP3A4, multiple UDP-glucuronosyltransferases (UGTs) and glutathione S-transferases (GSTs).	
	Active metabolites	Yes (minimal activity)

	Inactive metabolites	Yes
Elimination	No formal studies have been conducted, however selinexor is presumed to be excreted primarily into feces with minimal excretion into urine.	
	Half-life	6 to 8 hours

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C - Indications and Status

Health Canada Approvals:

- Multiple myeloma (MM)

Refer to the product monograph for a full list and details of approved indications

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D - Adverse Effects

Emetogenic Potential: Moderate

(In the BOSTON study (selinexor + bortezomib + dexamethasone), patients received a 5-HT3 receptor antagonist ± other antiemetics (e.g. olanzapine or NK1 RA) prior to and during treatment, and as needed after treatment.)

The following adverse effects were reported in ≥ 10 % of patients with relapsed or refractory MM in a Phase 3 study comparing selinexor, bortezomib, and dexamethasone (SVd) vs bortezomib and dexamethasone (Vd), where there was ≥ 2% increase from the comparator arm. Severe or life-threatening adverse effects (< 10%) are also included.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Gastrointestinal	Anorexia, weight loss (35%) (4% severe)	E
	Diarrhea (32%)	E
	Nausea, vomiting (50%) (8% severe)	I E

General	Fatigue (42%)	E
Hematological	Myelosuppression ± infection, bleeding (60%) (39% severe)	E D
Hepatobiliary	↑ LFTs (7%)	E
Metabolic / Endocrine	Abnormal electrolyte(s) (10%) (↓ or ↑ K, ↓ PO4, ↓ Ca, ↓ Na, ↓ Mg) (5% severe)	E
	Tumor lysis syndrome (rare)	I E
Nervous System	Cognitive disturbance (9%) (2% severe) (including confusion)	E
	Dizziness (12%)	E
	Dysgeusia (10%)	E
	Headache (10%)	E
Ophthalmic	Blurred vision (13%)	E D
	Cataract (22%)	E D
Renal	Nephrotoxicity (5%) (2% severe)	E
Respiratory	Cough, dyspnea (18%)	E

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for selinexor include myelosuppression ± infection, bleeding, nausea, vomiting, fatigue, anorexia, weight loss, diarrhea, cataract, cough, dyspnea, dizziness, and abnormal electrolyte(s).

Thrombocytopenia (60%) was the leading cause of dosage modifications in clinical trials. The median time to onset was 22 days for any grade and 43 days for Grade ≥ 3. Permanent discontinuation of treatment due to thrombocytopenia occurred in 2% of patients. Platelet transfusion and/or other treatments may be indicated in severe cases.

Neutropenia (15%) has occurred with selinexor. The median time to onset was 23 days for any grade and 40 days for Grade ≥ 3. Febrile neutropenia occurred in < 1% of patients.

Serious **infections** have occurred with selinexor, including pneumonia (14% severe), sepsis (4%) and upper respiratory tract infections (3.6% severe). Atypical fungal or herpes virus infections have also been reported.

New onset or worsening of **cataract,** which may require surgical removal, has been reported with selinexor with a median time to onset of approximately 8 months.

Severe **hyponatremia** has occurred with selinexor. The median time to onset was 21 days for any grade.

During clinical trials, severe **nausea/vomiting** and severe **diarrhea** were reported. The median time to onset was 6 days for nausea/vomiting; the median time to onset was 50 days for diarrhea.

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E - Dosing

Refer to protocol by which the patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Patients at risk of tumour lysis syndrome (i.e. high tumour burden) should have appropriate prophylaxis and be monitored closely.

Patients should maintain adequate fluid and caloric intake during treatment. Consider IV hydration for patients at risk of dehydration.

Adults:

Various dosing schedules are used depending on the indication. Refer to the product monograph or related regimen monographs for details.

In combination with bortezomib and dexamethasone:

Oral: 100 mg once weekly on Days 1, 8, 15, 22, 29; Q35 days

Dosage with Toxicity:

Dose Level	Selinexor Dose, mg once weekly*
0	100
-1	80
-2	60
-3	40
-4	Discontinue

*when used in combination with bortezomib and dexamethasone

Toxicity	Severity	Action
Thrombocytopenia	Grade 2 or 3	Reduce by 1 dose level.
	Grade 2 or 3, with bleeding	Hold until bleeding resolves. Administer platelet transfusions as per institutional practice. Restart at 1 dose level ↓.
	Grade 4	Hold until Grade ≤ 2. Restart at 1 dose level ↓.
Neutropenia	Grade 3	Reduce by 1 dose level.
	Grade 4	Hold until Grade ≤ 2. Restart at 1 dose level ↓.
Febrile neutropenia	Any	Hold until ANC returns to ≥ 1 x 10^9/L. Restart at 1 dose level ↓.
Anemia	Grade 3	Reduce by 1 dose level. Administer blood transfusions and/or other treatments as per institutional practice.
	Grade 4	Hold until Grade ≤ 2. Administer blood transfusions and/or other treatments as per institutional practice. Restart at 1 dose level ↓.
Nausea/vomiting	Grade 3 or 4	Hold until Grade ≤ 2. Start additional anti-emetics. Restart at 1 dose level ↓.
Diarrhea	Grade 2	Hold until Grade ≤ 1. Restart at same dose. If recurs, hold until Grade ≤ 1. Restart at 1 dose level ↓.
	Grade 3 or 4	Hold until Grade ≤ 1. Restart at 1 dose level ↓.
Weight loss and anorexia	Grade 2 (10-19% decrease from baseline weight) OR Anorexia associated with significant weight loss or malnutrition	Hold until weight returns to > 90% of baseline. Restart at 1 dose level ↓.

Hyponatremia	Grade 4 (Na < 120 mmol/L)	Hold until Na ≥ 130. Restart at 1 dose level ↓.
Fatigue	Grade 2, lasting > 7 days OR Grade 3	Hold until Grade ≤ 1. Restart at same dose. If recurs, hold until Grade ≤ 1. Restart at 1 dose level ↓.
Any new or worsening visual disturbance		Refer to ophthalmologist for evaluation.
Ocular (excluding cataract)	Grade 2	Hold until Grade ≤ 1. Refer to ophthalmologist for evaluation. Restart at 1 dose level ↓.
	Grade 3 or 4	Discontinue. Refer to ophthalmologist for evaluation.
Cataract	Grade 2, 3 or 4	Reduce by 1 dose level. Refer to ophthalmologist for evaluation. If surgery is warranted, hold dose 24 hours pre- and for 72 hours post-surgery.
Other non-hematologic	Grade 3 or 4	Hold until Grade ≤ 2. Restart at 1 dose level ↓.

Dosage with Hepatic Impairment:

Bilirubin		AST	Selinexor Dosage
≤ ULN	and	> ULN	No dose adjustment required.
>1 - 1.5 x ULN	and	Any	
>1.5 - 3 x ULN	and	Any	Caution; limited data.
>3 x ULN	and	Any	

Dosage with Renal Impairment:

No dose adjustments required in patients with mild to severe renal dysfunction (CrCl = 15 to 89 mL/min). There is no data in end-stage renal disease or hemodialysis.

Dosage in the elderly:

No overall differences in effectiveness were observed in patients ≥ 65 years compared to younger patients. Older patients had a higher incidence of serious adverse reactions and discontinuation due to adverse reactions.

Dosage based on gender:

No clinically significant differences were observed in the pharmacokinetics of selinexor based on sex.

Dosage based on ethnicity:

No clinically significant differences were observed in the pharmacokinetics of selinexor based on ethnicity.

Children:

Selinexor has not been studied in patients <18 years.

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F - Administration Guidelines

- Administer selinexor with or without food.
- Tablets should be swallowed whole with a glass of water. Do not break, chew, crush, or divide tablets.
- If a dose is missed, the patient should skip this dose and take the next dose as scheduled.
- If the patient vomits after a dose, the dose should not be repeated. Patients should take the next dose as scheduled.
- Store between 2 to 30°C.

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G - Special Precautions

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components

Other Warnings/Precautions:

- Severe hyponatremia or neurological toxicities, including life-threatening events, have occurred with selinexor.
- Patients should use caution when driving or operating a vehicle or potentially dangerous machinery as dizziness, confusion, and blurred vision have been reported.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Mutagenicity: No
- Clastogenicity: No
- Embryotoxicity: Yes
- Fetotoxicity: Yes
  Selinexor is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **1 week** after the last dose.
- Excretion into breast milk: Unknown
  Breastfeeding is not recommended, and for at least **1 week** after the last dose.
- Fertility effects: Probable

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H - Interactions

Selinexor is a minor substrate of CYP3A4. There is a potential drug interaction between selinexor and CYP3A4 inhibitors or inducers, however studies with strong CYP3A4 inhibitors did not show any clinically significant differences in pharmacokinetics of selinexor.

Selinexor is a substrate of UGTs and GSTs and inhibits OATP1B3, but does not inhibit other solute carrier (SLC) transporters.

AGENT	EFFECT	MECHANISM	MANAGEMENT
CYP3A4 inducers (i.e. phenytoin, rifampin, dexamethasone, carbamazepine, phenobarbital, St. John's Wort, etc)	↓ selinexor effect (theoretical)	↑ metabolism of selinexor	Monitor for efficacy when initiating therapy with concomitant moderate or strong CYP3A4 inducers.
Drugs that cause dizziness or mental status changes	↑ risk of neurological toxicity	Additive	Optimize concomitant medications to avoid exacerbating dizziness or mental status changes. Institute fall precautions as appropriate.

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
CBC	Baseline, before each cycle (more frequent during the first 3 months), and as clinically indicated
Electrolytes (including sodium*)	Baseline, before each cycle (more frequent during the first 2 months), and as clinically indicated
Weight, nutritional and hydration status	Baseline, before each cycle, and as clinically indicated
Liver function tests	Baseline and as clinically indicated
Renal function tests	Baseline and as clinically indicated
Clinical toxicity assessment for bleeding, infections, TLS, GI, ocular and neurologic effects.	At each visit

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

*Sodium levels may appear lower with concurrent hyperglycemia (serum glucose > 8.3 mmol/L) and high serum paraprotein levels; use corrected Na levels.

Suggested Clinical Monitoring

Monitor Type	Monitor Frequency
Blood glucose levels	Baseline and as clinically indicated

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J - Supplementary Public Funding

Exceptional Access Program (EAP Website)

- selinexor - In combination with bortezomib and dexamethasone for previously treated multiple myeloma

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K - References

Bahlis NJ, Sutherland H, White D, et al. Selinexor plus low-dose bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma.Blood.2018;132(24):2546-2554.

Center for Drug Evaluation and Research. Application Number 212306Orig1s000 Other Review(s). 1 7 2019.

Hing ZA, Fung HY, Ranganathan P, et al. Next-generation XPO1 inhibitor shows improved efficacy and in vivo tolerability in hematological malignancies. Leukemia. 2016 Dec;30(12):2364-2372.

Lassman AB, Wen PY, van den Bent MJ, et al. A Phase II Study of the Efficacy and Safety of Oral Selinexor in Recurrent Glioblastoma. Clin Cancer Res. 2022 Feb 1;28(3):452-60.

Lexicomp drug information: Selinexor. Accessed on February 6, 2024.

Mikhael J, Noonan KR, Faiman B, et al. Consensus Recommendations for the Clinical Management of Patients With Multiple Myeloma Treated With Selinexor. Clin Lymphoma Myeloma Leuk. 2020 Jun;20(6):351-357.

NCCN Guidelines®: Antiemesis. May 24, 2023.

Peterson TJ, Orozco J, Buege M. Selinexor: A First-in-Class Nuclear Export Inhibitor for Management of Multiply Relapsed Multiple Myeloma. Ann Pharmacother. 2020 Jun;54(6):577-582.

Prescribing Information: Xpovio® (selinexor). Karyopharm Therapeutics Inc. Mar 2022.

Product Monograph: Xpovio® (selinexor). Forus Therapeutics Inc. May 31, 2022.

Summary of Product Characteristics: Nexpovio (Selinexor). Stemline Therapeutics B.V. 13 May 2022.

March 2024 Updated Adverse effects section

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L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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