

5.21.130

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Last Review Date: March 6, 2026

Xpovio

Description

Xpovio (selinexor)

Background

Xpovio (selinexor) is a nuclear export inhibitor. Xpovio reversibly inhibits nuclear export of tumor suppressor proteins (TSPs), growth regulators, and mRNAs of oncogenic proteins by blocking exportin 1 (XPO1). XPO1 inhibition by Xpovio leads to accumulation of TSPs in the nucleus, reductions in several oncoproteins, such as c-myc and cyclin D1, cell cycle arrest, and apoptosis of cancer cells (1).

Regulatory Status

FDA-approved indications: Xpovio is a nuclear export inhibitor indicated: (1)

1. In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma (MM) who have received at least one prior therapy
2. In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.
3. 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.

Low platelet counts are common with Xpovio and can lead to bleeding which can be severe and can sometimes cause death. Monitor for low platelet counts and manage promptly. Low white blood cell counts are common with Xpovio and can sometimes be severe leading to increased

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risk of infection which can sometimes cause death. Monitor for low white blood cell counts and manage promptly. It is important for patients to drink enough fluids to help prevent dehydration and to eat enough calories to help prevent weight loss during treatment with Xpovio. Patients should be monitored for weight loss (1).

Xpovio also contains warnings for: thrombocytopenia, neutropenia, hyponatremia, gastrointestinal toxicity, neurological toxicity, embryo-fetal toxicity, cataract and serious infections (1).

Females of reproductive potential should be advised to avoid becoming pregnant while being treated, as Xpovio has been shown to cause fetal harm. Females of reproductive potential and males with a partner of reproductive potential should be advised to use effective contraception during treatment with Xpovio and for 1 week after the last dose (1).

The safety and effectiveness of Xpovio in patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xpovio may be considered **medically necessary** if the conditions indicated below are met.

Xpovio may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

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1. Multiple myeloma (MM)
 - a. Patient has received at least one prior therapy
 - b. Used in combination with bortezomib and dexamethasone
2. Relapsed or refractory multiple myeloma (RRMM)
 - a. Patient has received at least four prior therapies
 - b. Disease is refractory to at least two proteasome inhibitors (see Appendix 1)
 - c. Disease is refractory to at least two immunomodulatory agents (see Appendix 1)
 - d. Disease is refractory to an anti-CD38 monoclonal antibody (see Appendix 1)
 - e. Used in combination with dexamethasone
3. Relapsed or refractory diffuse large B-cell lymphoma (DLBCL)
 - a. Patient has received at least two prior lines of systemic therapy

AND ALL of the following:

- a. Patient will receive prophylactic treatment with a 5-HT3 antagonist (e.g., dolasetron, granisetron, ondansetron, palonosetron etc) and/or other anti-nausea agents prior to and during treatment with Xpovio
- b. Prescriber agrees to monitor complete blood count (CBC), standard blood chemistry, and body weight
- c. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Xpovio and for 1 week after the final dose
- d. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Xpovio and for 1 week after the final dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

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1. Multiple myeloma (MM)
 - a. Used in combination with bortezomib and dexamethasone
2. Relapsed or refractory multiple myeloma (RRMM)
 - a. Used in combination with dexamethasone
3. Relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

AND ALL of the following:

- a. **NO** disease progression or unacceptable toxicity
- b. Patient will receive prophylactic treatment with a 5-HT3 antagonist (e.g., dolasetron, granisetron, ondansetron, palonosetron etc) and/or other anti-nausea agents prior to and during treatment with Xpovio
- c. Prescriber agrees to monitor complete blood count (CBC), standard blood chemistry, and body weight
- d. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Xpovio and for 1 week after the final dose
- e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Xpovio and for 1 week after the final dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity Limit
10 mg tablets	96 tablets per 84 days
20 mg tablets	
40 mg tablets	
50 mg tablets	
60 mg tablets	
80 mg tablets	

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Weekly Dose	Strength per tablet	Carton	Blister Pack
40 mg <u>once</u> weekly	10 mg	4 blister packs (16 tablets total in the carton)	Each blister has four 10 mg tablets
40 mg <u>once</u> weekly	40 mg	4 blister packs (4 tablets total in the carton)	Each blister has one 40 mg tablet
40 mg <u>twice</u> weekly	40 mg	4 blister packs (8 tablets total in the carton)	Each blister has two 40 mg tablets
60 mg <u>once</u> weekly	60 mg	4 blister packs (4 tablets total in the carton)	Each blister has one 60 mg tablet
60 mg <u>twice</u> weekly	20 mg	4 blister packs (24 tablets total in the carton)	Each blister has six 20 mg tablets
80 mg <u>once</u> weekly	40 mg	4 blister packs (8 tablets total in the carton)	Each blister has two 40 mg tablets
80 mg <u>once</u> weekly	80 mg	4 blister packs (4 tablets total in the carton)	Each blister has one 80 mg tablet
80 mg <u>twice</u> weekly	20 mg	4 blister packs (32 tablets total in the carton)	Each blister has eight 20 mg tablets
100 mg <u>once</u> weekly	50 mg	4 blister packs (8 tablets total in the carton)	Each blister has two 50 mg tablets

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Xpovio (selinexor) is a nuclear export inhibitor. Xpovio reversibly inhibits nuclear export of tumor suppressor proteins (TSPs), growth regulators, and mRNAs of oncogenic proteins by blocking exportin 1 (XPO1). XPO1 inhibition by Xpovio leads to accumulation of TSPs in the nucleus, reductions in several oncoproteins, such as c-myc and cyclin D1, cell cycle arrest, and apoptosis of cancer cells. The safety and effectiveness of Xpovio in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Xpovio while maintaining optimal therapeutic outcomes.

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References

1. Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; October 2025.
2. NCCN Drugs & Biologics Compendium[®] Selinexor 2026. National Comprehensive Cancer Network, Inc. Accessed on January 15, 2026.

Policy History

Date	Action
July 2019	New addition
September 2019	Annual review
December 2019	Annual review
June 2020	Annual review
July 2020	Addition of indication: relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Updated dosing table
September 2020	Annual review
January 2021	Addition of indication: multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
March 2021	Annual review
May 2021	Revised quantity limits chart due to new tablet strengths and dosing packs. Added contraception requirement for female and male patients. Appendix 1 updated.
September 2021	Annual review and reference update
June 2022	Annual review and reference update
March 2023	Annual review and reference update
December 2023	Annual review and reference update
June 2024	Annual review and reference update
April 2025	Per PI update, addition of 10mg tablet and dosing pack
June 2025	Annual review and reference update
February 2026	Per PI update, added 80 mg tablets to quantity chart and updated blister pack availability
March 2026	Annual review and reference update

Keywords

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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.

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Appendix 1 - List of Multiple Myeloma Medications

Proteasome Inhibitors

Generic Name	Brand Name
carfilzomib	Kyprolis
ixazomib	Ninlaro
bortezomib	Velcade

Immunomodulatory Agents

Generic Name	Brand Name
pomalidomide	Pomalyst
lenalidomide	Revlimid
thalidomide	Thalomid

Anti-CD38 Monoclonal Antibody

Generic Name	Brand Name
daratumumab	Darzalex
daratumumab and hyaluronidase-fihj	Darzalex Faspro
isatuximab-irfc	Sarclisa