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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Antineoplastic Agents	**Original Policy Date:**	July 26, 2019
Subject:	Xpovio	**Page:**	1 of 7

Last Review Date: March 12, 2021

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 Indication: Xpovio is a nuclear export inhibitor indicated: (1)

1. In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma 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

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, severe anemia, hyponatremia, gastrointestinal toxicity, neurological toxicity, and 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 pediatric 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** in patients 18 years of age or older for the treatment of multiple myeloma, relapsed or refractory multiple myeloma or relapsed or refractory diffuse large B-cell lymphoma and when the conditions indicated below are met.

Xpovio is considered **investigational** for patients that are less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

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

1. Multiple myeloma
    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 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

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

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

1. Multiple myeloma
    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 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

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity Limit per 84 days
20 mg tablets*	96 tablets per 84 days

*Blister packs contain 20 mg tablets

Weekly dose	Strength per tablet	Carton	Blister Pack
80 mg twice weekly	20 mg	4 blister packs (32 tablets total in the carton)	Each blister has eight 20 mg tablets
60 mg twice weekly	20 mg	4 blister packs (24 tablets total in the carton)	Each blister has six 20 mg tablets
100 mg once weekly	20 mg	4 blister packs (20 tablets total in the carton)	Each blister has five 20 mg tablets
80 mg once weekly	20 mg	4 blister packs (16 tablets total in the carton)	Each blister has four 20 mg tablets
40 mg twice weekly	20 mg	4 blister packs (16 tablets total in the carton)	Each blister has four 20 mg tablets
60 mg once weekly	20 mg	4 blister packs (12 tablets total in the carton)	Each blister has three 20 mg tablets
40 mg once weekly	20 mg	4 blister packs (8 tablets total in the carton)	Each blister has two 20 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.

References

1. Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; December 2020.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on

March 12, 2021 and is effective on April 1, 2021.

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