Cigna National Formulary Coverage Policy

Effective Date..... 4/1/2023
Next Review Date..... 4/1/2024

Prior Authorization
Oncology – Xpovio® (selinexor tablets)

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Product Identifier(s)

62885

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

Cigna covers selinexor (Xpovio®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior Authorization is recommended for prescription benefit coverage of Xpovio. All approvals are provided for the duration noted below.

FDA Indication(s)

1. **Diffuse Large B-Cell Lymphoma.** Approve for 1 year if the individual meets BOTH of the following (A and B):
   Note: This includes individuals with histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma.
   A) Individual is ≥ 18 years of age; AND
   B) Individual has been treated with at least two prior systemic therapies.

2. **Multiple Myeloma.** Approve for 1 year if the individual meets ALL of the following (A, B, and C):
   - **A)** Individual is ≥ 18 years of age; AND
   - **B)** The medication will be taken in combination with dexamethasone; AND
   - **C)** Individual meets one of the following (i, ii, or iii):
     - **i.** Individual has tried at least four prior regimens for multiple myeloma; OR
     - **ii.** Individual meets both of the following (a and b):
       - **a)** Individual has tried at least one prior regimen for multiple myeloma; AND
       - **b)** The medication will be taken in combination with bortezomib; OR
     - **iii.** Individual meets both of the following (a and b):
       - **a)** Individual has tried at least one prior regimen for multiple myeloma; AND
         Note: Examples of prior regimens include bortezomib/Revlimid (lenalidomide capsules)/dexamethasone, Kyprolis (carfilzomib intravenous infusion)/Revlimid/dexamethasone, Darzalex (daratumumab intravenous infusion)/bortezomib or Kyprolis/dexamethasone, or other regimens containing a proteasome inhibitor, immunomodulatory drug, and/or anti-CD38 monoclonal antibody.
       - **b)** The medication will be taken in combination with Darzalex (daratumumab intravenous infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection), Kyprolis (carfilzomib intravenous infusion), or Pomalyst (pomalidomide capsules).

Conditions Not Covered

Selinexor (Xpovio®) is considered experimental, investigational or unproven for ANY other use.

Background

Overview

Xpovio, a nuclear export inhibitor, is indicated for treatment of the following conditions:[1]

- **Diffuse large B-cell lymphoma** (DLBCL), not otherwise specified (including DLBCL arising from follicular lymphoma), for treatment of relapsed or refractory disease in adults, after at least two lines of systemic therapy.
- **Multiple myeloma**:
  - In combination with dexamethasone for treatment of relapsed or refractory disease in adults 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.
  - In combination with bortezomib and dexamethasone, in adults who have received at least one prior therapy.

For DLBCL, Xpovio was approved under accelerated approval based on response rate. Continued approval may be contingent upon verification in a confirmatory trial(s).

Guidelines

Xpovio is addressed in the following guidelines from the National Comprehensive Cancer Network (NCCN):

- **B-Cell Lymphoma:** NCCN guidelines (version 2.2023 – February 8, 2023) recommend Xpovio as third-line and subsequent therapy of DLBCL (including for histologic transformation of indolent lymphomas to DLBCL), after at least two lines of systemic therapy.[3] This includes patients with disease progression after transplant or chimeric antigen receptor T-cell therapy.
- **Multiple Myeloma:** NCCN guidelines (version 3.2023 – December 8, 2022) recommend various regimens as primary therapy (transplant eligible and non-transplant candidates), maintenance therapy, and for previously treated multiple myeloma.[2] Xpovio/bortezomib/dexamethasone (once weekly) is among the "Other Recommended" regimens for previously treated disease following one to three previous therapies. Xpovio/dexamethasone after 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, is recommended for patients with late relapses (> three prior therapies). Xpovio/Darzalex® (daratumumab injection)/dexamethasone, Xpovio/Kyprolis® (carfilzomib intravenous infusion)/dexamethasone, and Xpovio/Pomalyst® (pomalidomide capsules)/dexamethasone are among

the regimens considered “Useful in Certain Circumstances” for previously treated multiple myeloma, for early relapses (one to three prior therapies).

References

1. Xpovio® tablets [prescribing information]. Newton, MA: Karyopharm Therapeutics; June 2022.
2. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 3.2023 – December 8, 2022). © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 26, 2023.
3. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2023 – February 8, 2023). © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 26, 2023.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	**Diffuse Large B-Cell Lymphoma:** A Note was added to clarify that this includes histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma.	03/01/2023