



PRIOR AUTHORIZATION POLICY

- POLICY:** Oncology – Xpovio Prior Authorization Policy
- Xpovio® (selinexor tablets – Karyopharm Therapeutics)

REVIEW DATE: 03/18/2026

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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xpovio, a nuclear export inhibitor, is indicated for the following uses: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 3.2026 – March 12, 2026) recommend Xpovio as third-line and subsequent therapy for DLBCL (including for histologic transformation of indolent lymphomas to DLBCL), high-grade-B-Cell lymphoma, human immunodeficiency virus-related B-Cell lymphoma, and post-transplant lymphoproliferative disorder (category 2A).² This includes patients with disease progression after transplant or chimeric antigen receptor (CAR) T-cell therapy.
- **Multiple Myeloma:** NCCN guidelines (version 5.2026 – January 9, 2026) recommend various regimens as primary therapy (transplant eligible and non-transplant candidates), maintenance therapy, and for previously treated multiple myeloma.³ Xpovio + dexamethasone is recommended for relapsed/refractory disease 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 (category 2A). The following recommendations are for relapsed/refractory disease after one to three prior therapies: Xpovio + bortezomib + dexamethasone (category 1 as “other recommended regimen”); Xpovio + Kyprolis[®] (carfilzomib intravenous infusion) + dexamethasone; Xpovio + Darzalex[®] (daratumumab intravenous infusion) + dexamethasone; and Xpovio + Pomalyst[®] (pomalidomide capsules) + dexamethasone (for patients who have received two prior therapies including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression on or within 60 days of completion of the last therapy) [all category 2A as “useful in certain circumstances”]. NCCN compendium states that Xpovio can be considered for multiple myeloma with central nervous system (CNS) disease as part of a multimodality treatment with intrathecal chemotherapy and radiation therapy (category 2A). The guidelines state that Xpovio can penetrate the blood brain barrier but has not been tested in the management of CNS disease in patients with multiple myeloma.

POLICY STATEMENT

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

- **Xpovio[®] (selinexor tablets – Karyopharm Therapeutics) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

FDA-Approved Indications

- 1. Diffuse Large B-Cell Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

Note: This includes patients with histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma.

- A)** Patient is \geq 18 years of age; AND
- B)** Patient has tried least two prior therapies.

2. Multiple Myeloma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

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

Other Uses with Supportive Evidence

- 3. B-Cell Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- A)** Patient is \geq 18 years of age; AND
 - B)** Patient has ONE of the following (i, ii, or iii):
 - i.** High-grade B-cell lymphoma; OR
 - ii.** Human immunodeficiency virus (HIV)-related B-cell lymphoma; OR
 - iii.** Post-transplant lymphoproliferative disorders; AND
 - C)** Patient has tried least two prior therapies.

CONDITIONS NOT COVERED

• **Xpovio® (selinexor tablets – Karyopharm Therapeutics) is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.**

REFERENCES

1. Xpovio® tablets [prescribing information]. Newton, MA: Karyopharm Therapeutics; October 2025.
2. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 3.2026 – March 12, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 12, 2026.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 5.2026 – January 9, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 12, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/06/2024
Annual Revision	<p>Diffuse Large B-Cell Lymphoma: The requirement that the patient has been treated with at least prior systemic therapies was reworded to patient has tried at least two prior therapies.</p> <p>Multiple Myeloma: A note with examples of a prior regimen was added for the requirement that patient has tried at least four prior regimens. The requirement that the patient has tried at least two prior regimens for multiple myeloma along with a note of examples of a prior regimen, and the medication will be taken in combination with Pomalyst (pomalidomide capsules) was added. Pomalyst (pomalidomide capsules) was removed from the list of medications that patient can use in combination with Xpovio if that have tried at least one prior regimen. The note with examples of prior regimen was modified to include Darzalex (daratumumab intravenous infusion)/bortezomib/lenalidomide/dexamethasone and mention of Revlimid was changed to the generic name lenalidomide.</p> <p>B-Cell Lymphoma. This condition and criteria for approval were added to Other Uses with Supportive Evidence.</p>	03/19/2025
Annual Revision	No criteria changes.	03/18/2026

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