Pharmacy Policy Bulletin: J-0254 Xpovio (selinexor) – Commercial and Healthcare Reform	
Number: J-0254	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0254-008	**Original Date:** 08/07/2019
Effective Date: 12/20/2024	**Review Date:** 12/04/2024

Drugs Product(s):	• Xpovio (selinexor)
FDA-Approved Indication(s):	• In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma (MM) who have received at least one prior therapy. • In combination with dexamethasone for the treatment of adult patients with relapsed or refractory MM 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. • 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.

Background:	• Xpovio reversibly inhibits nuclear export of tumor suppressor proteins (TSPs), growth regulators, and mRNAs of oncogenic proteins by blocking exportin 1 (XPO1). This inhibition leads to accumulation of TSPs in the cell nucleus, reduction in several oncoproteins, cell cycle arrest, and apoptosis of cancer cells. • For the treatment of MM in combination with bortezomib and dexamethasone, participants in the BOSTON study received one to three prior MM regimens (prior treatment with bortezomib or other PI was allowed). Previous courses of therapy included stem cell transplantation, lenalidomide, pomalidomide, bortezomib, carfilzomib, or daratumumab. • For the treatment of MM in combination with dexamethasone, the efficacy and safety of Xpovio was studied in a prespecified subgroup of patients whose disease was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide and daratumumab, as the benefit-risk ratio appeared to be greater in this more heavily pretreated population than in the overall trial population. • For the treatment of DLBCL, participants in the SADAL study received two to five prior treatment regimens before receiving Xpovio. Previous courses of therapy included anthracycline-based chemotherapy (unless contraindicated due to cardiac dysfunction—in this instance, other drugs such as etoposide,

	bendamustine, or gemcitabine were given) and at least one course of anti-CD20 immunotherapy, such as rituximab. • Prescribing Considerations: ○ Warnings and precautions include thrombocytopenia, neutropenia, gastrointestinal toxicity, hyponatremia, serious infections, neurological toxicity, embryo-fetal toxicity, and cataracts. ○ Xpovio should be prescribed under the supervision of a hematologist/oncologist.

Approval Criteria

I. Initial Authorization

A. Multiple Myeloma (MM)

1. In Combination with bortezomib and dexamethasone
When a benefit, coverage of Xpovio may be approved when all of the following criteria are met **(a. through d.)**:
- **a.** The member is 18 years of age or older.
- **b.** The member has a diagnosis of MM (ICD-10: C90).
- **c.** The member will use Xpovio in combination with bortezomib and dexamethasone.
- **d.** The member has received at least one (1) prior therapy for MM.

2. In Combination with dexamethasone
When a benefit, coverage of Xpovio may be approved when all of the following criteria are met **(a. through d.)**:
- **a.** The member is 18 years of age or older.
- **b.** The member has a diagnosis of relapsed or refractory MM (ICD-10: C90).
- **c.** The member will use Xpovio in combination with dexamethasone.
- **d.** The member has experienced therapeutic failure, contraindication, or intolerance to all of the following **(i., ii., and iii.):**
  - **i.** Two (2) proteasome inhibitors (e.g., bortezomib, carfilzomib).
  - **ii.** Two (2) immunomodulatory agents (e.g., lenalidomide, pomalidomide).
  - **iii.** One (1) anti-CD38 monoclonal antibody (e.g., daratumumab).

B. Diffuse large B-cell Lymphoma (DLBCL)
When a benefit, coverage of Xpovio may be approved when all of the following criteria are met **(1., 2., and 3.)**:
1. The member is 18 years of age or older.
2. The member has a diagnosis of relapsed or refractory DLBCL (ICD-10 C83.3).
3. The member has experienced therapeutic failure, contraindication, or intolerance to at least two (2) lines of systemic therapy.

II. Reauthorization
When a benefit, reauthorization of Xpovio may be approved when the following criterion is met **(A.)**:
- **A.** The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as either one (1) of the following **(1. or 2.)**:
  1. Disease improvement
  2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drugs addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; July 2022.