Clinical Policy: Selinexor (Xpovio)

Reference Number: ERX.SPA.342
Effective Date: 09.01.19
Last Review Date: 08.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Selinexor (Xpovio®) is a nuclear export inhibitor (XPO1 inhibitor).

FDA Approved Indication(s)
Xpovio is indicated:

- In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma (MM) who have received at least one prior therapy.
- For the treatment of adult patients with relapsed or refractory MM in combination with dexamethasone 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.
- For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS), including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Xpovio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all)**:**

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is relapsed, refractory, or progressive;
5. One of the following (a, b, c, d, or e):*
   a. Prescribed in combination with bortezomib and dexamethasone;
   b. Prescribed in combination with Darzalex®/Darzalex Faspro™ and dexamethasone;
   c. Prescribed in combination with carfilzomib and dexamethasone;
   d. Prescribed in combination with pomalidomide and dexamethasone and member has received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor;
   e. Prescribed in combination with dexamethasone and member has received ≥ 4 prior therapies (*see Appendix B)* including all of the following (i, ii, and iii):
      i. Two proteasome inhibitors (e.g., bortezomib, Kyprolis®, Ninlaro®);
      ii. Two immunomodulatory agents (e.g., Revlimid®, pomalidomide, Thalomid®);
      iii. One anti-CD38 monoclonal antibody (e.g., Darzalex);

**Prior authorization may be required for the agents listed above*

6. Request meets one of the following (a or b):*
   a. Dose does not exceed one of the following (i or ii):
      i. Prescribed in combination with bortezomib and dexamethasone: 100 mg (5 tablets) per week;
      ii. All other combination regimens: 160 mg (8 tablets) per week;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

B. Diffuse Large B-Cell Lymphoma (must meet all)**:**
1. Diagnosis of DLBCL, NOS, including DLBCL arising from follicular lymphoma or indolent lymphomas, AIDS-related DLBCL, primary effusion lymphoma, HHV8-positive DLBCL NOS;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is relapsed, refractory (no or partial response), or progressive;
5. Member has received ≥ 2 prior therapies* for relapsed or refractory disease (*see Appendix B*);

   **Prior authorization may be required*

6. Request meets one of the following (a or b):*
   a. Dose does not exceed 60 mg (3 tablets) twice weekly;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Xpovio for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For MM: New dose does not exceed one of the following (i or ii):
      i. Prescribed in combination with bortezomib and dexamethasone: 100 mg (5 tablets) per week;
      ii. All other combination regimens: 160 mg (8 tablets) per week;
   b. For DLBCL: New dose does not exceed 60 mg (3 tablets) twice weekly;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DLBCL: diffuse large B-cell lymphoma
FDA: Food and Drug Administration
MM: multiple myeloma
NCCN: National Comprehensive Cancer Network
NOS: not otherwise specified

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
MM: regimens containing proteasome inhibitors, immunomodulatory agents and/or anti-CD38 monoclonal antibodies (examples - NCCN)		
bortezomib / Revlimid (lenalidomide) or pomalidomide or Thalomid (thalidomide) / dexamethasone	Varies	Varies
Kyprolis (carfilzomib – weekly or twice weekly) / dexamethasone	Varies	Varies
Kyprolis / Revlimid / dexamethasone	Varies	Varies
Ninlaro (ixazomib) / Revlimid / dexamethasone	Varies	Varies
Darzalex (daratumumab) / bortezomib / dexamethasone ± Thalomid	Varies	Varies
Darzalex / Revlimid / dexamethasone	Varies	Varies
DLBCL NOS: second-line/subsequent regimens (examples - NCCN)		
GemOx (gemcitabine, oxaliplatin) ± rituximab	Varies	Varies
Polatuzumab vedotin ± rituximab ± bendamustine	Varies	Varies
DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab	Varies	Varies
DHAX (dexamethasone, cytarabine, oxaliplatin) ± rituximab	Varies	Varies
Yescarta® (axicabtagene ciloleucel)	Varies	Varies
Kymriah® (tisagenlecleucel)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	80 mg in combination with dexamethasone PO on days 1 and 3 of each week 100 mg in combination with bortezomib and dexamethasone PO on day 1 of each week	160 mg/week
DLBCL	60 mg taken PO on Days 1 and 3 of each week	60 mg/daily

VI. Product Availability

Tablets: 20 mg, 40 mg, 50 mg, 60 mg

VII. References

1. Xpovio Prescribing Information. Newton, MA: Karyopharm Therapeutics, Inc.; March 2022. Available at: https://www.xpovio.com/. Accessed April 28, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed April 28, 2022.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 5.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed April 28, 2022.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed April 28, 2022.
5. Kalakonda N, Maerevoet M, Cavallo F, et al. Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial. Lancet Haematol 2020; 7: e511–22.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.16.19	08.19
3Q 2020 annual review: criteria added for new FDA-approved indication: DLBCL; references reviewed and updated.	07.01.20	08.20
RT4: added new FDA approved indication in MM as second line therapy in combination with bortezomib and dexamethasone; added additional NCCN supported MM indications for use in combination with Darzalex and dexamethasone or pomalidomide and dexamethasone.	01.06.21	
3Q 2021 annual review: no significant changes; new 40 mg, 50 mg, 60 mg dosage forms added; references reviewed and updated.	05.11.21	08.21
3Q 2022 annual review: for MM added option for combination use with Darzalex Faspro, as well as carfilzomib and dexamethasone per NCCN; for DLBCL added additional DLBCL subtypes (e.g., histological transformation from indolent lymphomas, AIDS-related DLBCL, primary effusion lymphoma, HHV8-positive DLBCL NOS) , added additional descriptors for progressive disease and clarified refractory includes no or partial response to align with verbiage from NCCN compendium; references reviewed and updated.	04.28.22	08.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.