

## Clinical Policy: Selinexor (Xpovio)

Reference Number: ERX.SPA.342

Effective Date: 09.01.19

Last Review Date: 08.20

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 who have received at least one prior therapy.
- For the treatment of adult patients with relapsed or refractory multiple myeloma (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, or d):\*
  - a. Prescribed in combination with bortezomib and dexamethasone;
  - b. Prescribed in combination with Darzalex® and dexamethasone;
  - c. Prescribed in combination with pomalidomide and dexamethasone and member has received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor;
  - d. Prescribed in combination with dexamethasone and member has received ≥ 4 prior therapies (see Appendix B) including all of the following (a, b, and c):
    - 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®);
6. Request meets one of the following (a or b):\*

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

- 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;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. Disease is relapsed or refractory;
5. Member has received  $\geq$  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
<i>MM: regimens containing proteasome inhibitors, immunomodulatory agents and/or anti-CD38 monoclonal antibodies (examples - NCCN)</i>		
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
<i>DLBCL NOS: second-line/subsequent regimens (examples - NCCN)</i>		
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	160 mg/week
	100 mg in combination with bortezomib and dexamethasone PO on day 1 of each week	
DLBCL	60 mg taken PO on Days 1 and 3 of each week	60 mg/daily

**VI. Product Availability**

Tablet: 20 mg

**VII. References**

1. Xpovio Prescribing Information. Newton, MA: Karyopharm Therapeutics, Inc.; December 2020. Available at: <https://www.xpovio.com/>. Accessed January 6, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed January 6, 2021.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2021. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/myeloma.pdf](https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf). Accessed January 6, 2021.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2020. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/b-cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf). Accessed July 13, 2020.
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	

**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.

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