Clinical Policy: Selinexor (Xpovio)

Reference Number: CP.PHAR.431
Effective Date: 07.16.19
Last Review Date: 08.20
Line of Business: Commercial, HIM, 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 dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (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.
- 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.

These indications are approved under accelerated approval based on response rate. Continued approval for these indications 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.

It is the policy of health plans affiliated with Centene Corporation® 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 or refractory;
5. Member has received ≥ 4 prior therapies (*see Appendix B*) including all of the following (a, b, and c):
   a. Two proteasome inhibitors (e.g., bortezomib, Kyprolis®, Ninlaro®);*
   b. Two immunomodulatory agents (e.g., Revlimid®, pomalidomide, Thalomid®);*
   c. One anti-CD38 monoclonal antibody (e.g., Darzalex®);*
   **Prior authorization may be required*
6. Request meets one of the following (a or b):*

a. Dose does not exceed 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:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

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 ≥ 18 years;
4. Disease is relapsed or refractory;
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/HIM – 6 months
Commercial – Length of Benefit

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, 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 or b):*
   a. For MM: New dose does not exceed 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:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents

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 for all relevant lines of business 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
DLBCL	60 mg PO on Days 1 and 3 of each week	60 mg/day

VI. Product Availability
Tablet: 20 mg

VII. References
1. Xpovio Prescribing Information. Newton, MA: Karyopharm Therapeutics, Inc.; June 2020. Available at: https://www.karyopharm.com/wp-content/uploads/2019/07/NDA-212306-SN-0071-Prescribing-Information-01July2019.pdf. Accessed July 1, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 1, 2020.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 3.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed April 27, 2020.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2020. Available at: 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
Finalized line of businesses on policy to include HIM per SDC and prior clinical guidance.	12.02.19	
3Q 2020 annual review: criteria added for new FDA-approved indication: DLBCL; references reviewed and updated.	07.01.20	08.20

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.