

Clinical Policy: Selinexor (Xpovio)

Reference Number: CP.PHAR.431

Effective Date: 07.16.19

Last Review Date: 08.25

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 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.
- 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 confirmatory trial(s).

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 \geq 18 years;
4. For Xpovio requests, member must use selinexor, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Disease is relapsed, refractory, or progressive;
6. 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 Kyprolis[®] 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, iii, and iii):
 - i. Two proteasome inhibitors (e.g., bortezomib, Kyprolis, Ninlaro[®]);
 - ii. Two immunomodulatory agents (e.g., lenalidomide, pomalidomide, Thalomid[®]);
 - iii. One anti-CD38 monoclonal antibody (e.g., Darzalex[®]);
- *Prior authorization may be required for the agents listed above*
7. 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 (1 and 2):
 - 1) 100 mg per week;
 - 2) 5 tablets per week;
 - ii. All other combination regimens (1 and 2):
 - 1) 160 mg per week;
 - 2) 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 – 12 months

Commercial – 12 months or duration of request, whichever is less

B. B-Cell Lymphoma (must meet all):

1. Diagnosis of one of the following B-cell lymphomas (a, b, c, or d):
 - a. DLBCL, including DLBCL arising from indolent lymphomas;
 - b. High-grade B-cell lymphoma (off-label);
 - c. HIV-related B-cell lymphoma, including HIV-related DLBCL, primary effusion lymphoma, and HHV8-positive DLBCL NOS (off-label);
 - d. Monomorphic post-transplant lymphoproliferative disorder (B-cell type) (off-label);
 2. Prescribed by or in consultation with an oncologist or hematologist;
 3. Age ≥ 18 years;
 4. For Xpovio requests, member must use selinexor, if available, unless contraindicated or clinically significant adverse effects are experienced;
 5. Disease is relapsed, refractory (no or partial response), or progressive;
 6. Member has received ≥ 2 prior therapies* (*see Appendix B*);
**Prior authorization may be required*
 7. Request meets one of the following (a or b):*
 - a. Dose does not exceed (i and ii):
 - i. 120 mg per weekly;
 - ii. 6 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 – 12 months

Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 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. For Xpovio requests, member must use selinexor, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. 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 (1 and 2):
 - 1) 100 mg per week;
 - 2) 5 tablets per week;
 - ii. All other combination regimens (1 and 2):
 - 1) 160 mg per week;
 - 2) 8 tablets per week;
 - b. For B-cell lymphomas: New dose does not exceed (i and ii):
 - i. 120 mg per week;
 - ii. 6 tablets per week;
 - 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 – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 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.PA.154 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
<i>MM: regimens containing proteasome inhibitors, immunomodulatory agents and/or anti-CD38 monoclonal antibodies (examples - NCCN)</i>		
bortezomib / lenalidomide or pomalidomide or Thalomid (thalidomide) / dexamethasone	Varies	Varies
Kyprolis (carfilzomib – weekly or twice weekly) / dexamethasone	Varies	Varies
Kyprolis / lenalidomide / dexamethasone	Varies	Varies
Ninlaro (ixazomib) / lenalidomide / dexamethasone	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Darzalex (daratumumab) / bortezomib / dexamethasone ± Thalomid	Varies	Varies
Darzalex / lenalidomide / 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 PO on Days 1 and 3 of each week	60 mg/day

VI. Product Availability

Tablets: 10 mg, 20 mg, 40 mg, 50 mg, 60 mg, 80 mg

VII. References

1. Xpovio Prescribing Information. Newton, MA: Karyopharm Therapeutics, Inc.; October 2025. Available at: <https://www.xpovio.com>. Accessed January 28, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 28, 2026.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 13, 2025.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed May 13, 2025.
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
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
Added legacy WCG initial approval duration (WCG.CP.PHAR.431 to be retired); added oral oncology generic redirection language.	11.24.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
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
Template changes applied to other diagnoses/indications.	09.23.22	
3Q 2023 annual review: for DLBCL, removed follicular lymphoma, added high-grade B-cell lymphoma, and revised “AIDS-related” to “HIV-related” per NCCN; consolidated legacy WCG initial approval duration to standard Medicaid initial approval duration; references reviewed and updated.	04.14.23	08.23
3Q 2024 annual review: for DLBCL, revised header to the umbrella diagnosis of B-cell lymphoma and added monomorphic post-transplant lymphoproliferative disorder (B-cell type) per NCCN; references reviewed and updated.	05.16.24	08.24
RT4: added new 10 mg strength tablet; aligned B-cell lymphoma maximum dosing criteria from 60 mg twice a week to 120 mg per week and from 3 tablets twice a week to 6 tablets per week.	03.25.25	
3Q 2025 annual review: no significant changes; references reviewed and updated.	05.13.25	08.25
RT4: added new 80 mg strength tablet; extended Medicaid and HIM initial approval durations from 6 months to 12 months for this maintenance medication for a chronic condition.	01.28.26	

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.

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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.

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