BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

XPOVIO™ (selinexor) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for XPOVIO (selinexor)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by or in consultation with an Oncologist

Indication
- Multiple myeloma used in combination with bortezomib and dexamethasone after at least 1 prior therapy

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- Relapsed or refractory multiple myeloma (RRMM) used in combination with dexamethasone after at least 4 prior therapies and disease refractory to at least 2 proteasome inhibitors, at least 2 immunomodulatory agents, and an anti CD38 monoclonal antibody
- Relapsed or refractory diffuse large B cell lymphoma, not otherwise specified, including diffuse large B cell lymphoma arising from follicular lymphoma, after at least 2 lines of systemic therapy
- Other oncologic direct treatment use listed in National Comprehensive Cancer Network Guidelines with Categories of Evidence and Consensus of one or two A

Age Requirement

- 18 years or older

Baseline Clinical Evaluation

- Body weight
- Complete blood count with differential
- Standard blood chemistries
- Volume status
- Negative pregnancy test (if applicable)
- Eastern Cooperative Oncology Group Performance Status 0 to 2

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety

- Does not have end stage renal disease with Cockcroft Gault CrCl less than 15 milliliters per minute or on hemodialysis
- Does not have moderate to severe hepatic impairment

Documentation Requirements

- A completed request form must be submitted, including:
  - Chart notes
  - Lab results including all related lab values listed above
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

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Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications

- Continues to be seen by or in consultation with an Oncologist

Clinical Response

- No evidence of disease progression or unacceptable toxicity

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Has not developed significant adverse drug effects that exclude continued use, including:
  - Thrombocytopenia
  - Neutropenia
  - Nausea or vomiting
  - Diarrhea
  - Weight loss
  - Severe or life threatening hyponatremia
  - Severe ocular toxicity
  - Clinically severe bleeding
  - Four dose reductions for toxicity with unresolved toxicity
- Does not have end stage renal disease with Cockcroft Gault CrCl less than 15 milliliters per minute or on hemodialysis
- Does not have moderate to severe hepatic impairment

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in indication
- Lab values confirming safe continued use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

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Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Xpovio (selinexor) is an oral nuclear export inhibitor is indicated for the treatment of multiple myeloma (MM) used in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy and used in combination with dexamethasone in patients with relapsed or refractory MM who have received at least four prior therapies and whose disease is refractory to at least two proteosome inhibitors, at least two immunomodulatory agents and an anti-CD38 monoclonal antibody. It is also indicated for the treatment of 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. 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).

In nonclinical studies, selinexor reversibly inhibits nuclear export of tumor suppressor proteins (TSPs), growth regulators, and mRNAs of oncogenic proteins by blocking exportin 1 (XPO1, also known as chromosome region maintenance 1 [CRM1]). XPO1 is the major mammalian export protein that facilitates the transport of large macromolecules including RNA and protein across the nuclear membrane to the cytoplasm thereby facilitating proteins out of the nucleus. XPO1 inhibition by leads to accumulation of TSPs in the nucleus, reductions in several oncoproteins, such as c-myc and cyclin D1, cell cycle arrest, and apoptosis of cancer cells. Selinexor demonstrated pro-apoptotic activity in vitro in multiple myeloma cell lines and patient tumor samples, and in murine xenograft models.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Proteasome Inhibitors:
Velcade (bortezomib) injection
Kyprolis (carfilzomib) injection
Ninlaro (ixazomib) oral capsule

Anti-CD38 monoclonal antibody:
Darzalex (daratumumab) injection

Immunomodulatory agents:

Revlimid (lenalidomide)
Pomalyst (pomalidomide)
Thalomid (thalidomide)

An alkylating agent:
Bendamustine
Cisplatin
Cyclophosphamide
Alkeran (melphalan)

Other agents used in MM:
Adriamycin (doxorubicin)
Empliciti (elotuzumab)
Etoposide
Doxil (liposomal doxorubicin)
Farydak (panobinostat)

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences: urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

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Resources:

Xpovio (selinexor) product information, revised by Karyopharm Therapeutics, Inc. 03-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 11, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Multiple Myeloma Version 2.2025. Updated April 11, 2025. Available at https://www.nccn.org. Accessed May 10, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 2.2025. Updated February 10, 2025. Available at https://www.nccn.org. Accessed May 10, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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