BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

XPOVIO™ (selinexor) oral

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 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 precertification 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.

Criteria:

- **Criteria for initial therapy:** Xpovio (selinexor) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist.

  2. Individual is 18 years of age or older.

  3. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Used in combination with Velcade (bortezomib) and dexamethasone for the treatment of multiple myeloma (MM) in an individual who has received at least 1 prior therapy

     b. Used in combination with dexamethasone for the treatment of relapsed or refractory multiple myeloma (RRMM) in an individual who has received at least 4 prior therapies and whose disease

is refractory to at least 2 proteasome inhibitors, at least 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody

c. 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

d. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. The individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Body weight
   b. Negative pregnancy test in a woman of child-bearing potential
   c. Eastern Cooperative Oncology Group (ECOG) Performance Status is 0-2

5. Individual does not have end-stage renal disease (Cockcroft-Gault CrCl < 15 mL/min) or a patient on hemodialysis.

6. Individual does not have moderate to severe hepatic impairment.

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Xpovio (selinexor) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist.

2. Individual's condition has responded while on therapy with response defined as the following:
   a. No evidence of disease progression
   b. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication.

4. Individual has not developed any significant adverse drug effects that may exclude continued use:
   a. Thrombocytopenia, discontinuation is based on severity of reaction
   b. Neutropenia, discontinuation is based on severity of reaction
   c. Nausea/vomiting, discontinuation is based on severity of reaction
   d. Diarrhea, discontinuation is based on severity of reaction
   e. Weight loss, discontinuation is based on severity of reaction
   f. Hyponatremia, discontinuation is based on severity of reaction
   g. Severe ocular toxicity, discontinuation is
   h. There have been 3 dose reductions for toxicity and the toxicity still not resolved

5. Individual does not have end-stage renal disease (Cockcroft-Gault CrCl < 15 mL/min) or a patient on hemodialysis

6. Individual does not have moderate to severe hepatic impairment.

Renewal duration: 12 months

- 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:

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)

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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	

Resources:

Xpovio (selinexor) product information, revised by Karyopharm Therapeutics, Inc. 07-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 07, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Multiple Myeloma Version 5.2022 – Updated March 09, 2022. Available at https://www.nccn.org. Accessed August 04, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 5.2022 – Updated July 12, 2022. Available at https://www.nccn.org. Accessed August 05, 2022.

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.