BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**8/15/2019**
LAST REVIEW DATE:	**8/19/2021**
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XPOVIO™ (selinexor) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Xpovio (selinexor) is considered ***medically necessary*** and will be approved when **ALL** of 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. 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. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring 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. Will not be used in a patient with end-stage renal disease (Cockcroft-Gault CrCl < 15 mL/min) or a patient on hemodialysis

  6. Will not be used in a patient with moderate to severe hepatic impairment

  7. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Xpovio (selinexor) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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

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2. Individual's condition responded while on therapy
    a. Response is defined as:
        i. No evidence of disease progression
        ii. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Permanently discontinue for thrombocytopenia based on severity of reaction
        ii. Permanently discontinue for neutropenia based on severity of reaction
        iii. Permanently discontinue for nausea/vomiting based on severity of reaction
        iv. Permanently discontinue for diarrhea based on severity of reaction
        v. Permanently discontinue for weight loss based on severity of reaction
        vi. Permanently discontinue for hyponatremia based on severity of reaction
        vii. Permanently discontinue for severe non-cataract ocular toxicity
        viii. Permanently discontinue if had 3 dose reductions for toxicity and the toxicity still has not resolved

5. Will not be used in a patient with end-stage renal disease (Cockcroft-Gault CrCl < 15 mL/min) or a patient on hemodialysis

6. Will not be used in a patient with moderate to severe hepatic impairment

7. There are no significant interacting drugs

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 a Non-cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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

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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)

An alkylating agent:
- Bendamustine
- Cisplatin
- Cyclophosphamide
- Alkeran (melphalan)

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

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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. 04-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 28, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Multiple Myeloma Version 7.2021 – Updated April 26, 2021. Available at https://www.nccn.org. Accessed on June 28, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 4.2021 – Updated May 05, 2021. Available at https://www.nccn.org. Accessed on June 28, 2021.

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.