BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

OFF-LABEL USE OF CANCER MEDICATIONS

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 OFF-LABEL USE OF CANCER MEDICATIONS

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication
- Off-label use of a cancer medication for treatment of another cancer without a specific Pharmacy Coverage Guideline

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Age Requirement

- Age consistent with manufacturer recommendations, FDA approved labeling, or NCCN Guidelines

Baseline Clinical Evaluation

- Requested drug has at least one FDA-approved use for cancer
- Dose is consistent with manufacturer recommendations, FDA-approved labeling, or NCCN Guidelines

ONE of the following:

- The off-label use is recognized as safe and effective for the requested type of cancer and is listed and supported by NCCN Drugs & Biologics Compendium with Categories of Evidence and Consensus of 1 and 2A
- The off-label use is established from clinical trial(s) that have been published in peer reviewed professional medical journal(s) that has been submitted by the prescriber, and **ALL** the following apply:
  - At least **two** articles from major peer reviewed professional medical journals have recognized, based on scientific or medical criteria, the drug's safety and effectiveness for treatment of the indication for which the drug has been prescribed
  - No article from a major peer reviewed professional medical journal has concluded, based on scientific or medical criteria, that the drug is unsafe or ineffective or that the drug's safety and effectiveness cannot be determined for the treatment of the indication for which the drug has been prescribed
  - The literature meets the uniform requirements for manuscripts submitted to biomedical journals established by the international committee of medical journal editors or is published in a journal specified by the United States Department of Health and Human Services as acceptable peer reviewed medical literature pursuant to section 186(t)(2)(B) of the social security act (42 United States Code section 1395x(t)(2)(B))

Alternative Therapies

- Failure, contraindication, or intolerance to established therapies per NCCN is verifiably documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when 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

- No FDA-label contraindications for use of the requested drug
- No significant exclusions to use of the requested drug as outlined in product label (e.g., medical conditions, warnings or precautions for kidney dysfunction, hepatic dysfunction, etc.)
- No significant interacting drugs

Additional Requirements

- No benefit or contract exclusions that apply

Documentation Requirements

- A completed request form must be submitted, including:

- Chart notes
- Lab results
- Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 3 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)

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

Prescriber Qualification

- Continues to be seen by a physician specializing in or is 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 (when 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

- No new contraindications or significant adverse drug effects that may exclude continued use
- No significant exclusions to use of the requested drug as outlined in product label (e.g., medical conditions, warnings or precautions for kidney dysfunction, hepatic dysfunction, etc.)
- No significant interacting drugs

Additional Requirements

- No benefit or contract exclusions that apply

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

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OFF-LABEL USE OF CANCER MEDICATIONS

Criteria for Off-Label Use Requests:

Requests for **Off-label Use of Cancer medications** are considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:* Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration.

Description:

For FDA approved indications, also known as labeled indications, the FDA has reviewed and approved the medication for the specified use(s) for final marketing based on adequate, well-controlled clinical trials, which have documented safety and effectiveness. The use of an FDA approved medication for conditions, indications or in circumstances other than those approved by the FDA is known as “off-label use” (also referred to as unapproved use or unlabeled use). Unapproved or unlabeled uses include a variety of situations ranging from completely unstudied uses to scientifically investigated uses where the manufacturer has not asked the FDA for formal approval.

Off-label use of medications that have previously received FDA approval for marketing may be reviewed in any of the following ways: for medical necessity and/or investigational uses; during a review of a medication that requires prior authorization, during review of a medication due a non-formulary request for coverage, or during a review for any other prescription limitations.

An approved NDA (New Drug Application), ANDA (Abbreviated New Drug Application), or BLA (Biologic License Application) is considered final FDA-marketing approval for the purposes of this policy.

In certain instances, scientific evidence may support using a drug to treat a disease even if the drugs FDA approved label does not include those clinical conditions. In these circumstances, a compendia or scientific peer-reviewed literature specific for the indication in question may recommend uses beyond those included in the FDA approved labels. A compendium is a comprehensive listing of FDA approved drugs and biologics. Compendia include a summary of how each drug works in the body, as well as information for health care practitioners about proper dosing and whether the drug is recommended or endorsed for use in treating a specific disease.

Definitions:

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

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National Comprehensive Cancer Network (NCCN):
The National Cancer Comprehensive Network® (NCCN) Compendium is a free consensus-based guideline that lists the appropriate drugs and biologics for specific cancers using US Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category. http://www.nccn.org

Categories of Evidence and Consensus:

Category 1 recommendation	Based upon high-level evidence, there is uniform NCCN consensus that the recommendation is appropriate
Category 2A recommendation	Based upon lower-level evidence, there is uniform NCCN consensus that the recommendation is appropriate
Category 2B recommendation	Based upon lower-level evidence, there is NCCN consensus that the recommendation is appropriate
Category 3 recommendation	Based upon any level evidence, there is major NCCN disagreement that the recommendation is appropriate

For the 'uniform NCCN consensus' defined in Category 1 and Category 2A, a majority Panel vote of at least 85% is required. For the 'NCCN consensus' defined in Category 2B, a Panel vote of at least 50% (but less than 85%) is required. Lastly, for recommendations where there is strong Panel disagreement regardless of the quality of the evidence, NCCN requires a Panel vote of at least 25% to include and designate a recommendation as Category 3. The large majority of the recommendations put forth in the Guidelines are Category 2A. Where categories are not specified within the Guidelines, the default designation for the recommendation is Category 2A.

IBM Micromedex:

Efficacy, Strength of Evidence and Strength of Recommendation definitions:

Strength Of Recommendation		
Class I	Recommended	The given test or treatment has been proven to be useful, and should be performed or administered.
Class IIa	Recommended, In Most Cases	The given test, or treatment is generally considered to be useful, and is indicated in most cases.
Class IIb	Recommended, In Some Cases	The given test, or treatment may be useful, and is indicated in some, but not most, cases.
Class III	Not Recommended	The given test, or treatment is not useful, and should be avoided.
Class Indeterminate	Evidence Inconclusive	
Strength Of Evidence		
Category A	Evidence is based on data derived from: Meta-analyses of randomized controlled trials with homogeneity with regard to the directions and degrees of results between individual studies. Multiple, well-done randomized clinical trials involving large numbers of patients.	
Category B	Evidence is based on data derived from: Meta-analyses of randomized controlled trials with conflicting conclusions with regard to the directions and degrees of results between individual studies. Randomized controlled trials that involved small numbers of patients or had significant methodological flaws (e.g., bias, drop-out rate, flawed analysis, etc.). Nonrandomized studies (e.g., cohort studies, case-control studies, observational studies).	
Category C	Evidence is based on data derived from: Expert opinion or consensus, case reports or case series.	
No Evidence		
Efficacy		

Class I	Effective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is effective
Class IIa	Evidence Favors Efficacy	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion favors efficacy.
Class IIb	Evidence is Inconclusive	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion argues against efficacy.
Class III	Ineffective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is ineffective.

Resources:

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.