BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/17/2016
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 11/18/2021
ARCHIVE DATE:

OFF-LABEL USE OF CANCER MEDICATIONS

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.**

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/17/2016
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 11/18/2021
ARCHIVE DATE:

OFF-LABEL USE OF CANCER MEDICATIONS

Criteria:

- **Criteria for initial therapy:** An exception request for **Off-label Use of a *Cancer* medication** for the treatment of ***cancer*** without a specific Pharmacy Coverage Guideline may be 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. The requested agent has at least one FDA approved use for cancer

  3. **ONE** of the following:
     a. The off-label use is recognized as safe and effective for the requested type of cancer **and** that is listed **and** supported by:
        i. National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium with Categories of Evidence and Consensus of 1 and 2A

     b. 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** of the following apply:
        i. 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
        ii. 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
        iii. 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))

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

  5. There are no contraindications for use of the requested drug

  6. There are no significant interacting drugs

  7. There are no benefit or contract exclusions that apply

  Initial approval duration: 3 months

OFF-LABEL USE OF CANCER MEDICATIONS

- **Criteria for continuation of coverage (renewal request): Off-label Use of a Cancer medication** for the treatment of cancer without a specific Pharmacy Coverage Guideline is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation an Oncologist
  2. The condition has not progressed or worsened while on therapy
  3. The individual is adherent with the medication
  4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude to its continued use
  5. There are no significant interacting drugs
  6. There are no benefit or contract exclusions that apply

  Renewal duration: 12 months

- **Criteria when use is considered experimental or investigational:** The exception request is 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 Food and Drug Administration;
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes;
  3. Insufficient evidence to support improvement of the net health outcome;
  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 CANCER MEDICATIONS

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:

National Comprehensive Cancer Network (NCCN):

Categories of Evidence and Consensus:

Category 1 recommendation	Based upon high-level evidence, there is uniform NCN 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

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.	

OFF-LABEL USE OF CANCER MEDICATIONS

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.