BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
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ZYKADIA® (ceritinib) 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.**

ZYKADIA® (ceritinib) oral

Criteria:

- **Criteria for initial therapy:** Zykadia (ceritinib) 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. Non-small cell lung cancer (NSCLC) whose tumor is ALK fusion gene test that is anaplastic lymphoma kinase (ALK)-positive or ROS1 rearrangement-positive recurrent, advanced or metastatic

     b. 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. Fasting serum glucose
     b. Amylase and lipase
     c. Negative pregnancy test in a woman of child bearing age
     d. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2

  5. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Zykadia (ceritinib) 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 with an Oncologist

  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. The requested dose is at least 150 mg once daily

  5. Individual has not developed any significant adverse drug effects that may exclude continued use

a. Significant adverse effect such as:
   i. Confirmed interstitial lung disease or pneumonitis
   ii. Life-threatening bradycardia in those who are not taking a medication also known to cause bradycardia or known to cause hypotension
   iii. QTc interval prolongation such as Torsade de points or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia
   iv. ALT or AST elevation > 3x the upper limit of normal (ULN) with a total bilirubin elevation of > 2x the ULN in the absence of cholestasis or hemolysis
   v. Persistent hyperglycemia (> 250 mg/dL) despite anti-hyperglycemic medications

6. 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:

Zykadia (ceritinib) is a tyrosine kinase inhibitor, indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive by an FDA-approved test.

Protein kinases (PK) are a group of enzymes that modify other proteins by chemically adding a phosphate group from adenosine triphosphate (ATP) to a target molecule, usually on the serine, threonine, or tyrosine amino acid residues. PK can be subdivided or characterized by the amino acid that is phosphorylated: most PK act on both serine and threonine, tyrosine kinases act on tyrosine, and a number (dual-specificity kinases) act on all three. There are PK that phosphorylate other amino acids, such as histidine kinase that phosphorylates histidine residues. The human genome contains more than 500 PK (the human kinome) that have a role in inflammation, autoimmunity, and metabolism.

Phosphorylation results in a functional change of the target protein which in turn changes enzyme activity, cellular location, or association with other proteins. Processes regulated by phosphorylation include ion transport, cellular proliferation, differentiation, metabolism, migration, cellular survival, and hormone responses. Phosphorylation is a necessary step in some cancers and inflammatory diseases. Inhibition of protein kinase phosphorylation is a pharmacologic target that can be used to treat these disorders.

An inhibitor of protein kinase is a type of enzyme that specifically blocks the action of one or more PK. There are over 20 small molecule protein kinase inhibitors approved for the treatment of various conditions. Several

inhibitors have been successfully used to treat human cancers; these agents have been shown to inhibit multiple cellular functions of cancer cells, including proliferation, differentiation, survival, invasion, and angiogenesis.

Protein tyrosine kinases (PTK) play a key role in the regulation of cell proliferation, differentiation, metabolism, migration, and survival. Due to their involvement in various forms of cancers, PTK have become prominent targets for therapy.

Resources:

Zykadia (ceritinib) product information, revised by Novartis Pharmaceuticals Corporation 03-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 29, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 5.2021 – Updated June 15, 2021. Available at https://www.nccn.org. Accessed on June 29, 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.