

## PHARMACY COVERAGE GUIDELINE

### ZYKADIA® (ceritinib) oral

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#### **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](http://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](mailto:Pharmacyprecert@azblue.com).

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#### **Criteria:**

- **Criteria for initial therapy:** Zykadia (ceritinib) 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. Metastatic non-small cell lung cancer (NSCLC) whose tumor is anaplastic lymphoma kinase (ALK)-positive

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- 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. 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. 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. Individual is not using strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, others)
6. Individual does not consume grapefruit and grapefruit juice.

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Zykadia (ceritinib) 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:
    - 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's dose is at least 150 mg once daily.
  5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    - a. Confirmed interstitial lung disease or pneumonitis
    - b. Life-threatening bradycardia in those who are not taking a medication also known to cause bradycardia or known to cause hypotension
    - c. QTc interval prolongation such as Torsade de points or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia
    - d. 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
    - e. Persistent hyperglycemia (> 250 mg/dL) despite anti-hyperglycemic medications.
  6. Individual is not using strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, others).
  7. Individual does not consume grapefruit and grapefruit juice.

ORIGINAL EFFECTIVE DATE: 01/01/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 08/18/2022 | LAST CRITERIA REVISION DATE: 08/18/2022

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**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**
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#### **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.

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#### **Resources:**

Zykadia (ceritinib) product information, revised by Novartis Pharmaceuticals Corporation 10-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed August 07, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 3.2022 – Updated March 16, 2022. Available at <https://www.nccn.org>. Accessed August 07, 2022.



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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.

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