BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**3/13/2012**
LAST REVIEW DATE:	**5/19/2022**
LAST CRITERIA REVISION DATE:	**5/20/2021**
ARCHIVE DATE:	

XALKORI® (crizotinib)

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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XALKORI® (crizotinib)

Criteria:

- **Criteria for initial therapy:** Xalkori (crizotinib) 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. A confirmed diagnosis of **ONE** of the following:
     a. Adult (18 years of age or older) with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) rearrangement-positive or c-ros oncogene 1 (ROS-1) positive

     b. Pediatric patient 1 year of age or older (with a body surface area of at least 0.6 m^2) and young adult (less than or equal to 21 years of age) with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is ALK-positive (the safety and efficacy have not been established in older adults)

     c. 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

  3. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. Negative pregnancy test in a woman of childbearing potential
     b. Electrocardiogram (ECG) in individuals with a history of or predisposition for QTc prolongation, or who are taking medications that prolong QT
     c. Eastern Cooperative Oncology Group Performance status of 0-2

  Initial approval duration: 6 months

- **Criteria for continuation of continuation of coverage (renewal request):** Xalkori (crizotinib) 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

  2. Individual's condition responded while on therapy
     a. Response is defined as:
        i. No evidence of disease progression
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

  3. Individual has been adherent with the medication

  4. Individual has not developed any significant adverse drug effects that may exclude use
     a. Significant adverse effect such as:

i. Hepatotoxicity
ii. Interstitial lung disease/pneumonitis
iii. Individual on Xalkori who develops QTc > 500 ms or ≥ 60 ms change from baseline with Torsade de pointes, polymorphic ventricular tachycardia, or signs/symptoms of serious arrhythmia
iv. Life-threatening bradycardia due to Xalkori that is not associated with concomitant medications known to cause bradycardia or hypotension
v. Severe vision loss
vi. After dose reduction and recovery, a recurrence of neutropenia, thrombocytopenia, or anemia

5. The requested dose is at least 250 mg daily

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 Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Xalkori is an oral tyrosine kinase receptor inhibitor indicated for the treatment of individuals with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test and for metastatic NSCLC whose tumors are ROS1 rearrangement positive. Xalkori (crizotinib) is also indicated for the treatment of pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is ALK-positive. The safety and efficacy of Xalkori (crizotinib) have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL.

Detection of ALK-positive NSCLC using an FDA-approved test, indicated for this use, is necessary for selection of individuals for treatment with Xalkori. Assessment for ALK-positive NSCLC should be performed by laboratories with demonstrated proficiency in the specific technology being utilized. Improper assay performance can lead to unreliable test results. The FDA approved the Vysis ALK Break-Apart FISH Probe Kit (Abbott Molecular, Inc.) concurrently with the Xalkori approval. This companion diagnostic test is designed to detect rearrangements of the anaplastic lymphoma kinase (ALK) gene in NSCLC.

An FDA-approved test for the detection of the ROS1 rearrangements in NSCLC is not currently available. Identification of individuals with ROS1 rearrangements in NSCLC should use tests performed in the clinical study

of the drug. The study included individuals with histologically confirmed advanced NSCLC with ROS1 rearrangement. The ROS1 status of NSCLC tissue samples was determined by laboratory-developed break-apart FISH (96%) or RT-PCR (4%) clinical trial assays. For assessment by FISH, ROS1 positivity required that ≥15% of a minimum of 50 evaluated nuclei contained a ROS1 gene rearrangement.

Xalkori is an inhibitor of receptor tyrosine kinases including ALK, Hepatocyte Growth Factor Receptor (HGFR, c-Met), ROS1 (c-ros) and Recepteur d'Origine Nantais (RON). Translocations can affect the ALK gene resulting in the expression of oncogenic fusion proteins. The formation of ALK fusion proteins results in activation and dysregulation of the gene's expression and signaling which can contribute to increased cell proliferation and survival in tumors expressing these proteins.

Definitions:

NCCN Non-Small Cell Lung Cancer Guideline Version 4.2021:
Therapy for advanced or metastatic disease with ALK rearrangement positive tumor:

- First-line therapy:
  - Alecensa (alectinib)
  - Alunbrig (brigatinib)
  - Zykadia (ceritinib)
  - Xalkori (crizotinib)
  - Lorbrena (lorlatinib)
- Subsequent therapy:
  - Alecensa (alectinib)
  - Alunbrig (brigatinib)
  - Zykadia (ceritinib)
  - Lorbrena (lorlatinib)

Therapy for ROS1 rearrangement positive tumor:

- First-line therapy:
  - Zykardia (ceritinib)
  - Xalkori (crizotinib)
  - Rozlytrek (entrectinib)
- Subsequent therapy:
  - Rozlytrek (entrectinib)
  - Lorbrena (lorlatinib)

Resources:

Xalkori (crizotinib) product information, revised by Pfizer Laboratories Div Pfizer, Inc. 09-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2022.

XALKORI® (crizotinib)

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 May 13, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): T-Cell Lymphomas Version 2.2022 – Updated March 07, 2022. Available at https://www.nccn.org. Accessed May 13, 2022.

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.