BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

XALKORI® (crizotinib)
Generic Equivalent (if available)

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 XALKORI (crizotinib)

Criteria for Initial Therapy:

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

Indication
- Metastatic non small cell lung cancer (NSCLC) with tumors that are anaplastic lymphoma kinase (ALK) rearrangement positive or proto oncogene tyrosine protein kinase ROS (ROS 1) positive
- Relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is ALK positive
- Unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is ALK positive

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- Other oncologic direct treatment use listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement

- **For Metastatic NSCLC:** 18 years or older
- **For systemic ALCL**: 1 year or older with BSA at least 0.38 m² and young adults (less than or equal to 21 years of age)
- **For IMT:** 1 year or older with BSA at least 0.38 m²

Baseline Clinical Evaluation

- Presence of ALK or ROS1 positivity in tumor specimens in the treatment of metastatic NSCLC
- Ophthalmologic examination, including retinal examination, for pediatric and young adults with ALCL or pediatric patients with IMT
- Negative pregnancy test for women of childbearing potential
- Electrocardiogram (ECG) for individuals with history or predisposition for QTc prolongation or taking QT prolonging medications
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety

- No concomitant use with:
  - Strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, etc.)
  - Drugs that prolong QT interval (e.g., amiodarone, sotalol, quinidine, procainamide, levofloxacin, moxifloxacin, haloperidol, quetiapine, methadone, etc.)
  - Drugs that cause bradycardia (e.g., beta blockers, non dihydropyridine calcium channel blockers, clonidine, digoxin)

Additional Requirements

- Antiemetic and antidiarrheal agents are started prior to and during treatment of pediatric and young adult patients with ALCL or pediatric patients with IMT

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results (pregnancy test, ECG, ECOG status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

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Criteria for Continuation of Therapy (renewal therapy):

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

Prescriber Qualifications

- Continues to be seen by a physician specializing in or 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 (if 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 significant adverse drug effects such as:
  - ALT or AST greater than 3 times ULN with concurrent total bilirubin greater than 1.5 times ULN (in absence of cholestasis or hemolysis)
  - Interstitial lung disease/pneumonitis
  - QTc greater than 500 ms or change from baseline greater than or equal to 60 ms with serious arrhythmia
  - Life threatening bradycardia not associated with concomitant medications
  - Severe or life threatening vision loss
  - Severe nausea, vomiting, diarrhea, and stomatitis
  - Recurrence of neutropenia, thrombocytopenia, or anemia after dose reduction and recovery
  - Unable to tolerate Xalkori after 2 dose reductions for adverse reactions
- Requested dose is at least 250 mg daily
- No concomitant use with:
  - Strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, etc.)
  - Drugs that prolong QT interval (e.g., amiodarone, sotalol, quinidine, procainamide, levofloxacin, moxifloxacin, haloperidol, quetiapine, methadone, etc.)
  - Drugs that cause bradycardia (e.g., beta blockers, non dihydropyridine calcium channel blockers, clonidine, digoxin)

Documentation Requirements

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

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Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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. Xalkori is also indicated for the treatment of adult and pediatric patients 1 year of age and older with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is ALK-positive.

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.

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Definitions:

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

NCCN recommendation definitions:

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

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Resources:

Xalkori (crizotinib) product information, revised by Pfizer Laboratories Div Pfizer, Inc. 09-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed January 29, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-small Cell Lung Cancer Version 5.2026 – Updated March 13, 2026. Available at https://www.nccn.org. Accessed March 26, 2026.

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National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): T-Cell Lymphomas Version 2.2026 – Updated February 13, 2026. Available at https://www.nccn.org. Accessed March 26, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma Version 3.2026 – Updated March 12, 2026. Available at https://www.nccn.org. Accessed March 26, 2026.

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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