BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.21.12

Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Antineoplastic Agents	**Original Policy Date:**	February 24, 2012
Subject:	Xalkori	**Page:**	1 of 6

Last Review Date: March 12, 2021

Xalkori

Description

Xalkori (crizotinib)

Background
Xalkori (crizotinib) is an inhibitor of receptor tyrosine kinases including anaplastic lymphoma kinase (ALK), Hepatocyte Growth Factor Receptor (HGFR, c-Met), ROS1 (c-ros), and Recepteur d'Origine Nantais (RON). Detection of ALK-positive NSCLC using an FDA-approved test, such as the Vysis ALK Break-Apart FISH Probe Kit, is necessary for selection of patients for treatment with Xalkori (1-4).

Preliminary data indicate a presence of EML4-ALK in NSCLC is strongly associated with never or light smoking history. There is a significant relationship between smoking and *EML4-ALK* positivity, with the fusions more commonly found in light smokers (<10 pack years) or never smokers. At the histological level, the vast majority of lung tumors harboring EML4-ALK are adenocarcinomas (3).

Regulatory Status
FDA-approved indication: Xalkori is a kinase inhibitor indicated for the treatment of: (1)

- patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ALK or ROS1-positive as detected by an FDA-approved test
- 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

Limitations of Use: The safety and efficacy of Xalkori have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL (1).

Off Label Uses: (2-4)

1. Recurrence of non-small cell lung cancer (NSCLC) with ALK-positive tumors
2. NSCLC with MET amplification or MET exon 14 skipping mutation
3. Soft tissue sarcoma - Inflammatory myofibroblastic tumor (IMT) with ALK translocation

Drug-induced hepatotoxicity with fatal outcome has occurred. Temporarily suspend, dose reduce, or permanently discontinue Xalkori as indicated (1).

Xalkori has been associated with severe, life-threatening, or fatal treatment-related pneumonitis. Xalkori should be permanently discontinued in patients diagnosed with treatment-related pneumonitis. Complete blood counts including differential white blood cell counts should be monitored monthly and as clinically indicated, with more frequent repeat testing if Grade 3 or 4 abnormalities are observed, or if fever or infection occurs (1).

Xalkori should be avoided in patients with congenital long QT syndrome. In patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that are known to prolong the QT interval, periodic monitoring with electrocardiograms (ECGs) and electrolytes should be considered (1).

Severe visual loss has been reported in 0.2% of patients. Discontinue Xalkori in patients with severe visual loss. Perform ophthalmological evaluation (1).

Xalkori can cause fetal harm when administered to a pregnant woman based on its mechanism of action. Advise females of reproductive potential to use effective contraception during treatment with Xalkori and for at least 45 days following the final dose. Advise male patients with female partners of reproductive potential to use condoms during treatment with Xalkori and for at least 90 days after the final dose (1).

Safety and effectiveness in pediatric patients less than 18 years of age with NSCLC have not been established. Safety and effectiveness of Xalkori have not been established in pediatric patients younger than 12 months of age with ALCL (1).

Related policies

Alecensa, Alunbrig, Lorbrena, Zykadia

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xalkori may be considered **medically necessary** in patients with recurrent or metastatic non-small cell lung cancer (NSCLC); soft tissue sarcoma-inflammatory myofibroblastic tumor (IMT); or relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) and if the conditions indicated below are met.

Xalkori is considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

The patient must have **ONE** of the following:

1. Recurrent or metastatic non-small cell lung cancer (NSCLC)
    a. 18 years of age or older
    b. Patient must have **ONE** of the following:
        i. Tumor is positive for ALK mutation as determined by an FDA-approved test
        ii. Tumor is positive for ROS-1 mutation, as determined by an FDA-approved test
        iii. Tumor has MET amplification or MET exon 14 skipping mutation

2. Soft tissue sarcoma - Inflammatory myofibroblastic tumor (IMT)
    a. 18 years of age or older
    b. Tumor is positive for ALK mutation

3. Relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL)
    a. 1 to 21 years of age
    b. Tumor is positive for ALK mutation

AND ALL of the following:

1. Ophthalmology examination at baseline and periodically throughout treatment

2. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Xalkori and for at least 45 days after the last dose
3. Males with female partners of reproductive potential **only**: patient will be advised to use condoms during treatment with Xalkori and for at least 90 days after the last dose

Prior – Approval *Renewal* Requirements

Diagnoses

The patient must have **ONE** of the following:

1. Recurrent or metastatic non-small cell lung cancer (NSCLC)
    a. 18 years of age or older
2. Soft tissue sarcoma - Inflammatory myofibroblastic tumor (IMT)
    a. 18 years of age or older
3. Relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL)
    a. 1 to 21 years of age

AND ALL of the following:

1. **NO** symptoms indicative of treatment-related pneumonitis
2. Ophthalmology examinations are done periodically throughout treatment
3. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Xalkori and for at least 45 days following the final dose
4. Males with female partners of reproductive potential **only**: patient will be advised to use condoms during treatment with Xalkori and for at least 90 days after the final dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 360 capsules per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Xalkori (crizotinib) is an inhibitor of receptor tyrosine kinases including anaplastic lymphoma kinase (ALK), Hepatocyte Growth Factor Receptor (HGFR, c-Met), ROS1 (c-ros), and Recepteur d'Origine Nantais (RON). Xalkori has been associated with severe, life-threatening, or fatal treatment-related pneumonitis/ interstitial lung disease (ILD), hepatotoxicity, QT interval prolongation, and is contraindicated in pregnancy (1-4).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Xalkori (crizotinib) while maintaining optimal therapeutic outcomes.

References

1. Xalkori [package insert]. New York, NY: Pfizer Inc.; January 2021.
2. "National Comprehensive Cancer Network." *NCCN Drugs & Biologics Compendium*®. 2021.
3. NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 2.2021). National Comprehensive Cancer Network, Inc. December 2020.
4. NCCN Clinical Practice Guidelines in Oncology® Soft Tissue Sarcoma (Version 1.2021). National Comprehensive Cancer Network, Inc. October 2020.

Policy History

Date	Action
December 2011	New Policy
March 2013	Annual editorial review and reference update
June 2013	Labeled indications update and review.
December 2013	Annual editorial review and update
September 2014	Annual editorial review and update

December 2015	Annual editorial review and reference update
April 2016	Addition of recurrent non-small cell lung cancer (NSCLC) with one of the following: tumor is positive for ALK mutation, tumor is positive for ROS-1 mutation, or tumor has MET amplification or MET exon 14 skipping mutation; and in patient with soft tissue sarcoma - inflammatory myofibroblastic tumor (IMT) who have a tumor that is positive for ALK mutation; genetic mutations must be detected by FDA-approved test; ophthalmology examination at baseline and periodically throughout treatment; if patient or their partner are of child bearing age, the patient has been or will be instructed to practice effective contraception during therapy and for 2 months after stopping therapy Policy number changed from 5.04.12 to 5.21.12
June 2016	Annual review
June 2017	Annual editorial review and reference update. Addition age requirement to the renewal section Changed the use of effective contraception from 2 months after stopping therapy to 3 months after stopping therapy.
September 2017	Annual review Added quantity limits
June 2018	Annual editorial review and reference update
March 2019	Annual editorial review and reference update
June 2020	Annual review and reference update
February 2021	Addition of indication: relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL). Revised pregnancy requirements. Revised requirements so that only mutations with FDA-approved tests require it to be detected by an FDA-approved test
March 2021	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.