Xalkori (crizotinib)

Background
Xalkori is a kinase inhibitor indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. 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 patients with: (1)
   1. Metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test
   2. Metastatic NSCLC whose tumors are repressor of silencing (ROS-1) -positive

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. Liver function tests including ALT and total bilirubin should be monitored once a month and as clinically indicated, with more frequent testing in patients with Grade 2, 3, or 4 elevations. Temporarily suspend, dose reduce, or permanently discontinue Xalkori as indicated. Grade 2, 3, and 4 are defined by the Common Terminology Criteria for Adverse Effects (CTCAE) Grading System (1).

Xalkori has been associated with severe, life-threatening, or fatal treatment-related pneumonitis in clinical trials with a frequency of 1.6% that developed within 2 months after the initiation of treatment. 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. Dose interruption and/or reduction is recommended for patients exhibiting Grade 3 QTc prolongation (>500ms). Permanent discontinuation of Xalkori if Grade 3 QTc prolongation recurs or if patient develops Grade 4 QTc prolongation (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. There are no adequate and well controlled studies in pregnant women using Xalkori. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus. 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 final use (1).

Safety and efficacy in pediatric patients below the age of 18 have not been established (1).

Related policies
Alecensa, Avastin, Cyramza, Gilotrif, Iressa, Opdivo, Portrazza, Tagrisso, 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 age 18 years or age or older for recurrent or metastatic non-small cell lung cancer (NSCLC) or in patients with soft tissue sarcoma - inflammatory myofibroblastic tumor (IMT) and if the conditions indicated below are met.

Xalkori is considered investigational in patients below 18 years of age and for all other indications.

Prior-Approval Requirements

Age

18 years of age and older

Diagnoses

The patient must have ONE of the following:

1. Recurrent or metastatic non-small cell lung cancer (NSCLC) with ONE of the following:
   a. Tumor is positive for ALK mutation
   b. Tumor is positive for ROS-1 mutation
   c. Tumor has MET amplification or MET exon 14 skipping mutation

2. Soft tissue sarcoma - Inflammatory myofibroblastic tumor (IMT)
   a. Tumor is positive for ALK mutation

AND ALL of the following:

1. Genetic mutations must be detected by FDA-approved test
2. Ophthalmology examination at baseline and periodically throughout treatment
3. 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 3 months after stopping therapy
Prior – Approval Renewal Requirements

Age

18 years of age and older

Diagnoses

The patient must have ONE of the following:

1. Recurrent or metastatic non-small cell lung cancer (NSCLC)
2. Soft tissue sarcoma - Inflammatory myofibroblastic tumor (IMT)

AND ALL of the following:

1. NO symptoms indicative of treatment-related pneumonitis
2. Ophthalmology examination are done 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 3 months after stopping therapy

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval Renewal Limits

Duration 12 months

Rationale

Summary

Xalkori is a kinase inhibitor indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. Xalkori has been associated with severe, life-threatening, or fatal treatment-related pneumonitis, 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


Policy History

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<tr>
<td>March 2013</td>
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<td>April 2016</td>
<td>Addition of recurrent non-small cell lung cancer (NSCLC) with one of the</td>
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Keywords
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 22, 2017 and is effective on July 1, 2017.