Xalkori

Description

Xalkori (crizotinib)

Background
Xalkori is a kinase inhibitor indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive or ROS1 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 as detected by an FDA-approved test

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, 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 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 examinations are done 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

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**

**Quantity**

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<tr>
<th>Strength</th>
<th>Quantity per 90 days</th>
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<tr>
<td>200 mg</td>
<td>180 capsules per 90 days <strong>OR</strong></td>
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<tr>
<td>250 mg</td>
<td>180 capsules per 90 days <strong>OR</strong></td>
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**Duration** 12 months

**Prior – Approval *Renewal* Limits**

Same as above

**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 or ROS1 positive as detected by an FDA-approved test. 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

Policy History
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<thead>
<tr>
<th>Date</th>
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<tr>
<td>December 2011</td>
<td>New Policy</td>
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<tr>
<td>March 2013</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>June 2013</td>
<td>Labeled indications update and review.</td>
</tr>
<tr>
<td>December 2013</td>
<td>Annual editorial review and update.</td>
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<tr>
<td>September 2014</td>
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</tr>
<tr>
<td>December 2015</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>April 2016</td>
<td>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</td>
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<td>Subject:</td>
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Policy number changed from 5.04.12 to 5.21.12

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<tr>
<td>June 2017</td>
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<td>Addition age requirement to the renewal section</td>
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<td>Changed the use of effective contraception from 2 months after stopping therapy to 3 months after stopping therapy.</td>
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<td>September 2017</td>
<td>Annual review</td>
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<tr>
<td></td>
<td>Added quantity limits</td>
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<tr>
<td>June 2018</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>March 2019</td>
<td>Annual editorial review and reference update</td>
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**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 15, 2019 and is effective on April 1, 2019.