



EXPRESS SCRIPTS®

## PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology – Xalkori® (crizotinib capsules – Pfizer)

**TAC APPROVAL DATE:** 12/19/2018

---

### OVERVIEW

Xalkori, an oral kinase inhibitor, is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.<sup>1</sup> Xalkori is also FDA-approved for the treatment of patients with metastatic NSCLC whose tumors are ROS1-positive.

Rearrangements involving the ALK locus on chromosome 2p33 have been documented in approximately 50% of inflammatory myofibroblastic tumors (IMTs).<sup>7</sup> IMTs occur primarily during the first two decades of life and typically arise in the lung, retroperitoneum, or abdominal region. Local recurrence may occur after initial surgery, with a low risk of distant metastases. Sustained partial response to Xalkori in a patient *with* ALK-translocated IMT, and no observed activity in a patient *without* ALK translocation have been reported. In another case report, a 45-year old Hispanic female was eventually diagnosed to have IMT with systemic involvement and ALK gene rearrangement.<sup>8</sup> The patient was treated with Xalkori and had a successful resolution of her lesions and symptoms. After a 27-month follow-up, the patient remained in complete clinical and radiologic remission.

### Guidelines

According to the National Comprehensive Cancer Network (NCCN) NSCLC guidelines (version 2.2019), Xalkori, Zykadia™ (ceritinib capsules), Alecensa® (alectinib capsules) and Alunbrig™ (brigatinib tablets) are all of the recommended first-line therapies for ALK-positive NSCLC (all category 1).<sup>2</sup> For subsequent therapy with progression on Xalkori, local therapy can be considered, Xalkori can be continued, or therapy can be switched to Zykadia, (if not previously given) Alecensa (if not previously given), or Alunbrig [category 2A] for asymptomatic progression or symptomatic progression to the brain. If there is rapid radiographic progression or threatened organ function, continuing Xalkori therapy is not recommended and instead alternate therapies should be considered. The guidelines also refer to NCCN guidelines for CNS Cancers for additional therapies. For multiple systemic lesions, Zykadia (if not previously given and progression on Xalkori initial therapy), Alecensa (if not previously given and progression on Xalkori initial therapy), or Alunbrig (all category 2A) are recommended or other cytotoxic therapy options (i.e., chemotherapy) can be used. For progression on Alecensa, Alunbrig, or Zykadia, Lorbrina (lorlatinib tablets) is recommended (category 2A). Xalkori or Zykadia are recommended as first-line therapy for ROS1 rearrangement-positive NSCLC (both category 2A). Of the two choices, Xalkori is preferred. Lorbrina can be used as subsequent therapy for ROS1 rearrangement. Xalkori is also recommended as an emerging targeted therapy in patients with high level *MET* amplification or *MET* exon 14 skipping mutation in lung cancer (category 2A).

### POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Xalkori. All approvals are provided for 3 years unless otherwise noted below.

**Automation:** None.

---

12/19/2018

© 2018 Express Scripts Holding Company. All Rights Reserved.

This document is confidential and proprietary to Express Scripts Holding Company. Unauthorized use and distribution are prohibited.

### **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Xalkori is recommended in those who meet the following criteria:

#### **FDA-Approved Indications**

- 1. Non-Small Cell Lung Cancer (NSCLC).** Approve for 3 years if the patient has metastatic anaplastic lymphoma kinase (ALK)-positive NSCLC as detected by an approved test.
- 2. Non-Small Cell Lung Cancer (NSCLC) with ROS1 Rearrangement.** Approve for 3 years.

#### **Other Uses with Supportive Evidence**

- 3. Non-Small Cell Lung Cancer (NSCLC) with High Level *MET* Amplification or *MET* Exon 14 Skipping Mutation.** Approve for 3 years.

The NCCN guidelines for NSCLC recommend Xalkori for patients with high level *MET* amplification or *MET* exon 14 skipping mutation (category 2A).<sup>2</sup> There are limited data available with Xalkori use in patients with NSCLC and *MET* amplification.<sup>3-5</sup>

- 4. Soft Tissue Sarcoma Inflammatory Myofibroblastic Tumor (IMT) with ALK Translocation.** Approve for 3 years.

The NCCN guidelines for soft tissue sarcoma (version 2.2018) recommend Xalkori as single-agent therapy for the treatment of IMT with ALK translocation (category 2A recommendation).<sup>6</sup>

- 5. Peripheral T-Cell Lymphoma – Anaplastic Large Cell Lymphoma (ALCL), ALK-Positive.** Approve for 3 years if Xalkori is used as a single agent for second-line and subsequent therapy in patients with intention to proceed and no intention to proceed to transplant.

The NCCN T-Cell lymphoma guidelines (version 1.2019) recommend Xalkori use in ALK-positive ALCL as a second-line and subsequent therapy option (category 2A) in patients with intent to proceed to transplant and in those who do not intend to proceed to transplant.<sup>9-10</sup> In one Phase II trial 26 patients, divided in two cohorts based on dose, with relapsed/refractory ALK-positive ALCL received Xalkori twice daily at doses of 165 mg/m<sup>2</sup> and 280 mg/m<sup>2</sup>.<sup>11</sup> The overall response rate were 83% and 90% for the two dose-ranging cohorts, respectively. Complete response was observed in 83% of patients in the lower-dose cohort and in 80% of the patients in the higher dose cohort.

### **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Xalkori has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.**

## References

1. Xalkori® capsules [prescribing information]. New York, NY: Pfizer Inc; April 2017.
2. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 2.2019 – November 21, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed December 14, 2018.
3. Ou S-HI, Kwak EL, Siwak-Tapp C, et al. Activity of crizotinib (PF02341066), a dual mesenchymal-epithelial transition (MET) and anaplastic lymphoma kinase (ALK) inhibitor, in a non-small cell lung cancer patient with de novo MET amplification. *J Thorac Oncol*. 2011;6:942-946.
4. Schwab R, Petak I, Kollar M, et al. Major partial response to crizotinib, a dual MET/ALK inhibitor, in a squamous cell lung carcinoma (SCC) patient with de novo c-MET amplification in the absence of ALK rearrangement. *Lung Cancer*. 2014;83:109-111.
5. Paik PK, Drilon A, Yu H, et al. Response to MET inhibitors in patients with stage IV adenocarcinomas harboring MET mutations causing exon 14 skipping. *Cancer Discov*. 2015;5:842-849.
6. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (Version 2.2018 – March 27, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed December 14, 2018.
7. Butrynski JE, D'Adamo DR, Hornick JL, et al. Crizotinib in ALK-rearranged inflammatory myofibroblastic tumor. *N Engl J Med*. 2010;363(18):1727-1733.
8. Jacob SV, Reith JD, Kojima AY, et al. An unusual case of systemic inflammatory myofibroblastic tumor with successful treatment with ALK-inhibitor. *Case Rep Pathol*. 2014;2014:470340.
9. The NCCN T-Cell lymphomas Clinical Practice Guidelines in Oncology (Version 1.2019 – November 21, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed December 14, 2018.
10. The NCCN Drugs & Biologics Compendium. © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on: December 14, 2018. Search term: crizotinib.
11. Mosse YP, Voss SD, Lim MS, et al. Targeting ALK with crizotinib in pediatric anaplastic large cell lymphoma and inflammatory myofibroblastic tumor: a Children's Oncology Group Study. *J Clin Oncol*. 2017;35:3215-3221.

## HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Selected revision	Approval duration extended from 12 months to 3 years	09/03/2014
Annual revision	Changed indication to match prescribing information and added new criteria for approval in NSCLC with MET amplification based on NCCN guidelines.	12/03/2014
Annual revision	Under Other Uses with Supportive Evidence, deleted approval criteria for patients already started on Xalkori therapy without a genetic test to line up with other targeted therapies criteria. Also, the MET amplification indication wording and the soft tissue sarcoma indication wording were modified to match up with how they are stated in NCCN guidelines. Deleted condition listed under Conditions Not Recommended for Approval section since it is a duplicate of what is listed in other parts of the criteria.	12/16/2015
DEU revision	Moved approval for ROS1 rearrangement from “Other uses with supportive evidence” to “FDA-approved indications.” No criteria changes. Also updated NCCN guidelines.	03/22/2016
Annual revision	No criteria changes	12/14/2016
Annual revision	Added approval criteria in patients with ALK+ anaplastic large cell lymphoma based on NCCN T-Cell lymphomas guideline recommendations.	12/13/2017
Annual revision	No criteria changes	12/19/2018

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; \* For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; ALK – Anaplastic lymphoma kinase; NCCN – National Comprehensive Cancer Network.