Clinical Policy: Crizotinib (Xalkori)

Reference Number: CP.PHAR.90
Effective Date: 11/11
Last Review Date: 08/17 Revision_Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for crizotinib (Xalkori®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Xalkori is **medically necessary** when one of the following criteria is met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all):

1. Diagnosis of non-small cell lung cancer (NSCLC);
2. Member meets a or b:
   a. FDA approved use (i and ii):
      i. Disease is metastatic;
      ii. Tumor is ROS1- or anaplastic lymphoma kinase (ALK)-positive;
   b. Off-label NCCN recommended use:
      i. Tumor is positive for high level MET amplification or an MET exon 14 skipping mutation;
3. Prescribed dose does not exceed 500 mg/day.

Approval duration: 6 months

B. Other diagnoses/indications:

1. Uses outlined in the NCCN compendium and which meet NCCN categories 1 or 2a are covered for the following indications:
   a. Inflammatory myofibroblastic tumor (IMT) [a soft tissue sarcoma] with ALK translocation.

II. Continued Approval

A. Non-Small Cell Lung Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy (e.g., no disease progression or unacceptable toxicity);
3. Prescribed dose does not exceed 500 mg/day and is not < 250 mg/day.

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Crizotinib 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. Crizotinib demonstrated concentration-dependent inhibition of ALK, ROS1, and c-Met phosphorylation in cell-based assays using tumor cell lines and demonstrated antitumor activity in mice bearing tumor xenografts that expressed EML4- or NPM-ALK fusion proteins or c-Met.

Formulations:

Xalkori oral capsules: 200 mg, 250 mg

FDA Approved Indications:

Xalkori is a receptor tyrosine kinase inhibitor/oral capsule formulation indicated for:

- Treatment of patients with metastatic NSCLC whose tumors are ALK-positive as detected by an FDA-approved test.
- Treatment of patients with metastatic NSCLC whose tumors are ROS1-positive.

Appendices

Appendix A: Abbreviation Key

ALK: anaplastic lymphoma kinase
ALT: alanine aminotransferase
AST: aspartate aminotransferase
IMT: inflammatory myofibroblastic tumor
NSCLC: non-small cell lung cancer

Reviews, Revisions, and Approvals	Date	Approval Date
Converted embedded SGM document into Centene policy	08/13	
Updated safety profile to include hematologic toxicity & bradycardia, revised hepatotoxicity, interstitial lung disease and QI interval. Added adverse event and dose modification tables. Clarified FDA approval for metastatic disease and removed locally advanced, and added dosing modifications to drug algorithm. Updated references.	02/14	03/14
Added pregnancy category and treatment duration	01/15	02/15

Reviews, Revisions, and Approvals	Date	Approval Date
Added recommendation for severe renal impairment in body of Safety section Updated statistical information for 2015 Added NCCN guideline recommendation to background Removed "Is patient responding to Xalkori therapy?" from Figure 1 Added "More than one systemic lesion found?" to Figure 1 for all patients currently receiving therapy Removed "Will the dose be adjusted according to Table 1 or 2?" from Figure 1 Changed "Experiencing any adverse events listed in Table 1?" to "Has the patient experienced an adverse event requiring permanent discontinuation?" in Figure 1		
Policy converted to new template. Criteria: added age. Background: limited to description/MOA and FDA approved indication. Appendices: removed safety appendix requiring discontinuation – inserted safety information directly into re-auth criteria set. References: limited to PI and NCCN NSCLC; NCCN data used in re-auth criteria for evidence of multiple systemic symptomatic lesions in presence of progression.	01/16	02/16
Criteria: Added new indication for ROS1-positive NSCLC per PI. Added NCCN recommendations for use. Removed age and prescriber restriction. Removed the criteria regarding presence of lesion. Background: added formulations.	06/16	08/16
Maximum and minimum doses added. Reasons to discontinue removed. Approval periods increase from 3/6 to 6/12 months.	07/17	08/17

References

1. Xalkori Prescribing Information. New York, NY: Pfizer, Inc.; April 2017. Available at http://labeling.pfizer.com/showlabeling.aspx?id=676. Accessed July 5, 2017.
2. Crizotinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed July 5, 2017.
3. Non-small cell lung cancer (Version 7.2017). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed July 5, 2017.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or

administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs,LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.

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