Evolent Clinical Guideline 3207 for Xalkori™ (crizotinib)

Guideline Number:	Applicable Codes	
Evolent_CG_3207		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
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STATEMENT

Purpose

To define and describe the accepted indications for Xalkori (crizotinib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Anaplastic Large Cell Lymphoma (ALCL)

- Xalkori (crizotinib) may be used as a single agent for members 21 years old or younger with relapsed/refractory Anaplastic Large Cell Lymphoma that is:
    - Positive for ALK: Anaplastic Lymphoma Kinase (confirmed by testing prior to initiation of treatment) AND
    - The member has experienced disease progression on at least one prior therapy.

Non-Small Cell Lung Cancer (NSCLC)

- The member has locally advanced, recurrent, or metastatic NSCLC and Xalkori (crizotinib) may be used as a single agent for ROS1 or ALK rearrangement positive tumors (confirmed by testing prior to initiation of treatment) as first line or subsequent therapy.

Soft Tissue Carcinoma – Inflammatory Myofibroblastic Tumor (IMT) with ALK Translocation

- Xalkori (crizotinib) may be used as a single agent for adult and pediatric members 1 year of age and older with inflammatory myofibroblastic tumor (IMT) that is ALK fusion positive, confirmed prior to treatment.

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Xalkori (crizotinib) is being used concurrently with chemotherapy.
- Absence of documented ROS1/ALK testing and results of such testing for the above indications.
- Dosing exceeds single dose limit of Xalkori (crizotinib) 250 mg (for NSCLC); 500 mg (for ALCL and IMT).
- Treatment exceeds the maximum limit of:
  - 120 (250 mg) or 120 (200 mg) capsules a month, or
  - 120 (20 mg), 120 (50 mg), or 180 (150 mg) oral pellets a month
- Investigational use of Xalkori (crizotinib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
  - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J8999 - crizotinib

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
November 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1206 Xalkori (crizotinib) • Updated exclusion criteria • Updated references
November 2024	• Updated dosage forms, and added oral pellet strengths to exclusion criteria • Updated maximum dosage form quantities in exclusion criteria • Updated references

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Solomon BJ, et al; PROFILE 1014 Investigators. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. *N Engl J Med*. 2014 Dec 4;371(23):2167-77. doi: 10.1056/NEJMoa1408440.
2. Shaw AT, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. *N Engl J Med*. 2013 Jun 20;368(25):2385-94. doi: 10.1056/NEJMoa1214886.
3. Shaw AT, et al. Crizotinib in ROS1-rearranged advanced non-small-cell lung cancer (NSCLC): updated results, including overall survival, from PROFILE 1001. *Ann Oncol*. 2019 Jul 1;30(7):1121-1126. doi: 10.1093/annonc/mdz131.
4. Foster JH, et al. Activity of Crizotinib in Patients with ALK-Aberrant Relapsed/Refractory Neuroblastoma: A Children's Oncology Group Study (ADVL0912). *Clin Cancer Res*. 2021 Jul 1;27(13):3543-3548. doi: 10.1158/1078-0432.CCR-20-4224.
5. Gambacorti-Passerini C, et al. Long-term effects of crizotinib in ALK-positive tumors (excluding NSCLC): A phase 1b open-label study. *Am J Hematol*. 2018 May;93(5):607-614. doi: 10.1002/ajh.25043.
6. Xalkori prescribing information. Pfizer Labs. New York, NY 2023.
7. Clinical Pharmacology Elsevier Gold Standard 2025.
8. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
9. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
10. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
11. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
12. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
13. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.