Clinical Policy: Crizotinib (Xalkori)

Reference Number: CP.PHAR.90
Effective Date: 11.01.11
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Crizotinib (Xalkori®) is a kinase inhibitor.

FDA Approved Indication(s)

Xalkori is indicated for the treatment of:

- Adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test.
- Pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is ALK-positive.*
- Adult and pediatric patients 1 year of age and older with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is ALK-positive.

*Limitation(s) of use: The safety and efficacy of Xalkori have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

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

1. Diagnosis of recurrent, advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is ALK, ROS1, MET exon 14 skipping, or high-level MET amplification positive;
5. Prescribed in one of the following ways (a or b):
   a. As a single agent;
   b. For high-level MET amplification positive NSCLC with an existing EGFR mutation: Xalkori can be administered with continuation of Tagrisso®;
6. For Xalkori requests, member must use generic crizotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):

i. 500 mg per day;
ii. One of the following (1 or 2):
1) 2 capsules per day;
2) 6 pellets per day;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Anaplastic Large Cell Lymphoma (must meet all)**:**

1. Diagnosis of ALCL (a peripheral T-cell lymphoma);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 1 year;
4. Disease is ALK-positive;
5. Prescribed as a single agent;
6. Prescribed as treatment for one of the following (a or b):
   a. Palliative intent;
   b. Relapsed or refractory disease;
7. For Xalkori requests, member must use generic crizotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 560 mg/m^2 per day, up to a maximum of 1,000 mg per day;
      ii. Either of the following (1 or 2):
         1) 4 capsules per day;
         2) 8 pellets per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Inflammatory Myofibroblastic Tumor (must meet all)**:**

1. Diagnosis of IMT;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 1 year;
4. Disease is ALK-positive;
5. Prescribed as a single agent;
6. For Xalkori requests, member must use generic crizotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a, b, or c):*
   a. For pediatric members, dose does not exceed both of the following (i and ii):
      i. 560 mg/m^2 per day, up to a maximum of 1,000 mg per day;
      ii. Either of the following (1 or 2):

1) 4 capsules per day;
2) 8 pellets per day;

b. For adult members, dose does not exceed both of the following (i and ii):
i. 500 mg per day;
ii. Either of the following (1 or 2):
1) 2 capsules per day;
2) 6 pellets per day;

c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Off-Label NCCN Compendium Recommended Indications (must meet all)**:**

1. Prescribed for one of the following diagnoses (a - c):
   a. Histiocytic neoplasm (Erdheim-Chester Disease, Langerhans Cell Histiocytosis, Rosai-Dorfman Disease);
   b. Cutaneous melanoma;
   c. Uterine IMT that is advanced, recurrent, metastatic, or inoperable;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For histiocytic neoplasm or uterine sarcoma, disease is ALK-positive;
5. For cutaneous melanoma, all of the following (a, b, and c):
   a. Disease is metastatic or unresectable;
   b. Disease is ROS1-positive;
   c. Xalkori is prescribed as second-line or subsequent therapy;
6. Prescribed as a single agent;
7. For Xalkori requests, member must use generic crizotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).**

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

E. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Xalkori for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Xalkori requests, member must use generic crizotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. NSCLC and adult IMT: New dose does not exceed both of the following (i and ii):
      i. 500 mg per day;
      ii. Either of the following (1 or 2):
         1) 2 capsules per day;
         2) 6 pellets per day;
   b. ALCL and pediatric IMT: New dose does not exceed both of the following (i and ii):
      i. 560 mg/m^2 per day, up to a maximum of 1,000 mg per day;
      ii. Either of the following (1 or 2):
         1) 4 capsules per day;
         2) 8 pellets per day;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALK: anaplastic lymphoma kinase
ALCL: anaplastic large cell lymphoma
FDA: Food and Drug Administration
IMT: inflammatory myofibroblastic tumor
MET: mesenchymal-epithelial transition
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer
ROS1: ROS proto-oncogene 1

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Cutaneous Melanoma		
Opdivo® (nivolumab) ± Yervoy® (ipilimumab)	Varies	Varies
Opdivo® (nivolumab) + Opdualag® (relatlimab-rmbw)	Varies	Varies
Keytruda® (pembrolizumab)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- MET amplification is an oncogenic driver occurring in 1% to 5% of NSCLCs that confers a poor prognosis. High-level MET amplification is an emerging biomarker to identify novel therapies for patients with metastatic NSCLC per NCCN. The definition of high-level MET amplification is evolving and may differ according to the assay used for testing. For results based on next-generation sequencing, a gene copy number greater than 10 is consistent with high-level MET amplification.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NSCLC	250 mg PO BID	500 mg/day
ALCL	280 mg/m^2 PO BID	1,000 mg/day
IMT	Pediatric: 280 mg/m^2 PO BID Adult: 250 mg PO BID	Pediatric: 1,000 mg/day Adult: 500 mg/day

VI. Product Availability

Capsules: 200 mg, 250 mg
Oral pellets: 20 mg, 50 mg, 150 mg

VII. References

1. Xalkori Prescribing Information. New York, NY: Pfizer, Inc.; September 2023. Available at http://labeling.pfizer.com/showlabeling.aspx?id=676. Accessed January 16, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 19, 2025.
3. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 2.203.202524. Available at www.nccn.org. Accessed February 19, 2025.
4. National Comprehensive Cancer Network Guidelines. Soft Tissue Sarcoma Version 1.2025. Available at www.nccn.org. Accessed February 19, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: RT4: updated with FDA-approved indication for ALCL (previously included as an NCCN supported off-label use) with age 1 year or older and dosing limits per label; oral oncology generic redirection language added; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	01.12.21	05.21
2Q 2022 annual review: for NSCLC, clarified criteria as MET as exon 14 skipping or high-level MET amplification positive per NCCN; added hematologist as specialist in ALCL; added criterion for Xalkori single-agent therapy for NSCLC, ALCL, and inflammatory myofibroblastic tumor per NCCN; added histiocytic neoplasms indications per NCCN category 2A; WCG.CP.PHAR.90 was retired and initial approval duration was consolidated to 6 months; Commercial approval durations revised from "Length of Benefit" to	02.14.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
"12 months or duration of request, whichever is less"; references reviewed and updated.		
RT4: updated criteria for new FDA approved indication of IMT and removed previous designation as off-label.	07.27.22	
Template changes applied to other diagnoses/indications.	10.12.22	
2Q 2023 annual review: added off-label NCCN-supported indications of cutaneous melanoma and uterine sarcoma; references reviewed and updated.	02.04.23	05.23
RT4: added new oral pellet dose form per updated prescribing information; added indication specific quantity limits for pellets.	09.12.23	
2Q 2024 annual review: added palliative treatment option for ALCL per NCCN; condensed uterine sarcoma IMT-specific criteria; references reviewed and updated.	01.12.24	05.24
2Q 2025 annual review: added option for combination with continued Tagrisso if member has high-level MET amplification and an EGFR mutation per NCCN Compendium; references reviewed and updated	02.19.25	05.25

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.