PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Xalkori Prior Authorization Policy
- Xalkori® (crizotinib capsules and oral pellets – Pfizer)

REVIEW DATE: 01/17/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xalkori, an oral kinase inhibitor, is indicated for the following uses:[1]

- **Anaplastic large cell lymphoma (ALCL)**, treatment of relapsed or refractory, systemic ALCL that is anaplastic lymphoma kinase (*ALK)*-positive in pediatric patients ≥ 1 year of age and young adults.
- **Inflammatory Myofibroblastic tumor (IMT),** treatment of unresectable, recurrent, or refractory IMT that is *ALK*-positive in patients ≥ 1 year of age.
- **Non-small cell lung cancer (NSCLC)**, metastatic, whose tumors are *ALK*-positive or c-*rOS* proto-oncogene 1 (*ROS1)*-positive as detected by an FDA-approved test in adults.

Guidelines

Xalkori has been addressed in National Comprehensive Cancer Network (NCCN) guidelines:[5-8]

- **Histiocytic Neoplasms:** Guidelines (version 1.2023 – August 11, 2023) recommend Xalkori as a "useful in certain circumstances" treatment option for the following types of histiocytic neoplasm with *ALK* rearrangement/fusion: Langerhans cell histiocytosis, Erdheim-Chester disease, and Rosai-Dorfman disease (category 2A).[3]

- **Inflammatory Myofibroblastic Tumor (IMT):** NCCN Soft Tissue Sarcoma guidelines (version 3.2023 – December 12, 2023) and NCCN Uterine Neoplasms guidelines (version 1.2024 – September 20, 2023) recommend Xalkori as a treatment option for IMT with *ALK* translocation.[4,5]
- **Melanoma: Cutaneous:** Guidelines (version 3.2023 – October 27, 2023) recommend Xalkori as a treatment option for cutaneous melanoma with *ALK* or *ROS1* fusions.[6] Case reports or limited clinical trial data have suggested activity for various gene fusions; Xalkori is noted for *ROS1* and *ALK* fusions.
- **NSCLC:** Guidelines (version 1.2024 – December 21, 2023) recommend Xalkori as a treatment option for *ROS1* rearrangement, *ALK* rearrangement-positive NSCLC, and as a treatment option for NSCLC with mesenchymal-epithelial transition (*MET*) exon 14 skipping mutation or high-level *MET* amplification.[7]
- **T-Cell Lymphoma:** Guidelines (version 1.2024 – December 21, 2023) recommend Xalkori as a treatment option for *ALK*-positive ALCL either as initial palliative-intent therapy or for relapsed or refractory disease.[7] NCCN notes that Xalkori also demonstrated activity in adults with relapsed or refractory *ALK*-positive ALCL, after at least one line of prior cytotoxic therapy.[8]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xalkori. All approvals are provided for the duration noted below.

- **Xalkori® (crizotinib capsules and oral pellets (Pfizer)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Anaplastic Large Cell Lymphoma.** Approve for 1 year if the patient meets the following (A, B, and C):
   A) Patient is ≥ 1 year of age; AND
   B) Patient has anaplastic lymphoma kinase (*ALK*)-positive disease; AND
   C) Patient meets one of the following (i or ii):
      i. The medication is used for palliative-intent therapy; OR
      ii. Patient has relapsed or refractory disease.

2. **Inflammatory Myofibroblastic Tumor.** Approve for 1 year if the patient meets the following (A, B, and C):
   A) Patient is ≥ 1 year of age; AND
   B) Patient has anaplastic lymphoma kinase (*ALK*)-positive disease; AND
   C) Patient meets one of the following (i or ii):
      i. Patient has advanced, recurrent, or metastatic disease; OR
      ii. The tumor is inoperable.

3. **Non-Small Cell Lung Cancer – Anaplastic Lymphoma Kinase (*ALK*)-Positive.** Approve for 1 year if the patient meets the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has advanced or metastatic disease; AND
   C) Patient has anaplastic lymphoma kinase (*ALK*)-positive disease; AND
   D) The mutation was detected by an approved test.

4. **Non-Small Cell Lung Cancer – *ROS1* Rearrangement-Positive.** Approve for 1 year if the patient meets the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has advanced or metastatic disease; AND
   C) Patient has *ROS1* rearrangement-positive disease; AND
   D) The mutation was detected by an approved test.

Other Uses with Supportive Evidence

5. **Histiocytic Neoplasm.** Approve for 1 year if patient meets the following (A, B, and C).
   A) Patient is ≥ 18 years of age; AND
   B) Patient has anaplastic lymphoma kinase (*ALK*) rearrangement/fusion-positive disease; AND
   C) Patient meets one of the following (i, ii, or iii):
      i. Patient has Langerhans cell histiocytosis; OR
      ii. Patient had Erdheim-Chester disease; OR
      iii. Patient has Rosai-Dorfman disease.

6. **Melanoma, Cutaneous.** Approve for 1 year if patient meets the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets one of the following (i or ii):
      i. Patient has anaplastic lymphoma kinase (*ALK*) fusion disease; OR
      ii. Patient has *ROS1* fusion disease.

7. **Non-Small Cell Lung Cancer with Mesenchymal Epithelial Transition (*MET) M*utation.** Approve for 1 year if the patient meets the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets one of the following (i or ii):
      i. Patient has non-small cell lung cancer with high level *MET* amplification; OR
      ii. Patient has non-small cell lung cancer with *MET* exon 14 skipping mutation.

CONDITIONS NOT COVERED

- **Xalkori® (crizotinib capsules and oral pellets (Pfizer)**

is(are) considered experimental, investigational, or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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 and oral pellets [prescribing information]. New York, NY: Pfizer; September 2023.
2. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 12, 2024. Search term: crizotinib.
3. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2023 – August 11, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2024.
4. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 3.2023 – December 12, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2023.
5. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – September 20, 2023) © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2023.
6. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 3.2023 – October 27, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2024.
7. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – December 21, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2024.
8. The NCCN T-Cell lymphomas Clinical Practice Guidelines in Oncology (version 1.2024 – December 21, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Inflammatory Myofibroblastic Tumor:** The following requirements were added: Patient is ≥ 1 year of age; Patient has advanced, recurrent, or metastatic disease or the tumor is inoperable. The requirement that the patient has anaplastic lymphoma kinase (*ALK*)-positive disease was moved from the condition of approval and into the criteria. Previously, the criteria approved for Inflammatory Myofibroblastic Tumor with *ALK* Translocation with no additional requirements. **Melanoma, cutaneous:** This new condition of approval was added to the policy.	01/11/2023
Selected Revision	Added oral pellets formulation of Xalkori to the policy.	11/22/2023
Annual Revision	**Anaplastic Large Cell Lymphoma:** Added criterion that the medication can be used for palliative-intent therapy based on guideline recommendations.	01/17/2024