

Xalkori® (crizotinib) (Oral)

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I. Length of Authorization

Coverage is provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Xalkori 200 mg capsules: 60 capsules per 30 days (2 capsules per day)
- Xalkori 250mg capsules: 60 capsules per 30 days (2 capsules per day)

B. Max Units (per dose and over time) [HCPCS Unit]:

- All indications: 500 mg per day

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age, unless otherwise specified; **AND**

Universal Criteria ¹

- Must be used as single agent; **AND**
- Patient will avoid concomitant therapy with all of the following:
 - Coadministration with strong or moderate CYP3A inhibitors (e.g., ketoconazole, clarithromycin, grapefruit juice, aprepitant, diltiazem, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
 - Coadministration with strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
 - Coadministration with drugs that prolong the QT-interval (e.g., fluoroquinolone or macrolide antibiotics, venlafaxine, fluoxetine, quetiapine, ziprasidone, sumatriptan, zolmitriptan, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

- Coadministration with drugs that cause bradycardia (e.g., beta-blockers, non-dihydropyridine calcium channel blockers, clonidine, digoxin, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

Non-Small Cell Lung Cancer (NSCLC) † ‡ ◻^{1,2,5-7,11}

- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrent or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
 - Patient has anaplastic lymphoma kinase (ALK) positive disease as detected by an FDA-approved or CLIA compliant test◊; **OR**
 - Patient has ROS-1 rearrangement positive disease as detected by an FDA-approved or CLIA compliant test◊; **OR**
 - Patient has MET exon 14 skipping mutation positive tumors; **OR**
- Patient has metastatic disease with high level MET amplification

Inflammatory Myofibroblastic Tumor (IMT) – Soft Tissue Sarcoma ‡^{2,4,9}

- Patient has anaplastic lymphoma kinase (ALK) positive disease

Anaplastic Large Cell Lymphoma (ALCL) † ‡^{1-3,10}

- Patient is at least 1 year of age; **AND**
- Patient has anaplastic lymphoma kinase (ALK) positive disease as detected by an FDA-approved or CLIA compliant test◊; **AND**
- Used as subsequent therapy for relapsed or refractory disease

◊ *If confirmed using an immunotherapy assay* <http://www.fda.gov/companiondiagnostics>

† FDA Approved Indication(s); ‡ Compendia recommended indication(s); ◻ Orphan Drug

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hepatotoxicity (severe changes in liver function tests), interstitial lung disease/pneumonitis, QT prolongation, bradycardia, severe vision loss, gastrointestinal toxicity in patients with ALCL, etc.

V. Dosage/Administration ^{1,8,9}

Indication	Dose												
Non-Small Cell Lung Cancer	250 mg orally twice daily until disease progression or unacceptable toxicity.												
Inflammatory Myofibroblastic Tumor	250 mg orally twice daily until disease progression or unacceptable toxicity.												
Anaplastic Large Cell Lymphoma	<p>280 mg/m² orally twice daily until disease progression or unacceptable toxicity.</p> <p>The recommended dosage is based on body surface area (BSA) as indicated in the table below:</p> <table border="1"> <thead> <tr> <th>Body Surface Area *</th> <th>Recommended Xalkori Dose</th> </tr> </thead> <tbody> <tr> <td>0.60 – 0.80 m²</td> <td>200 mg orally twice daily</td> </tr> <tr> <td>0.81 – 1.16 m²</td> <td>250 mg orally twice daily</td> </tr> <tr> <td>1.17 – 1.51 m²</td> <td>400 mg orally twice daily</td> </tr> <tr> <td>1.52 – 1.69 m²</td> <td>450 mg orally twice daily</td> </tr> <tr> <td>1.70 m² or greater</td> <td>500 mg orally twice daily</td> </tr> </tbody> </table> <p>* The recommended dosage for patients with a BSA less than 0.60 m² has not been established.</p>	Body Surface Area *	Recommended Xalkori Dose	0.60 – 0.80 m ²	200 mg orally twice daily	0.81 – 1.16 m ²	250 mg orally twice daily	1.17 – 1.51 m ²	400 mg orally twice daily	1.52 – 1.69 m ²	450 mg orally twice daily	1.70 m ² or greater	500 mg orally twice daily
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VI. Billing Code/Availability Information

HCPCS Code:

- J8999: Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

NDC:

- Xalkori 200 mg capsule - 00069-8141-xx
- Xalkori 250 mg capsule - 00069-8140-xx

VII. References

1. Xalkori [package insert]. New York, NY; Pfizer, Inc; January 2021. Accessed January 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) for Crizotinib. National Comprehensive Cancer Network, 2021. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2021.

3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) T-Cell Lymphomas. Version 1.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2021.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Soft Tissue Sarcoma. Version 1.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2021.
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7. Shaw AT, Ou SH, Bang YJ, et al. Crizotinib in ROS1-rearranged non-small-cell lung cancer. *N Engl J Med.* 2014 Nov 20;371(21):1963-71. doi: 10.1056/NEJMoa1406766. Epub 2014 Sep 27.
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10. Mossé YP, Lim MS, Voss SD, et al. Safety and activity of crizotinib for paediatric patients with refractory solid tumours or anaplastic large-cell lymphoma: a Children's Oncology Group phase 1 consortium study. *Lancet Oncol.* 2013 May;14(6):472-80. doi: 10.1016/S1470-2045(13)70095-0.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Non-Small Cell Lung Cancer. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C84.60	Anaplastic large cell lymphoma, ALK-positive, unspecified site
C84.61	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of head, face, and neck
C84.62	Anaplastic large cell lymphoma, ALK-positive, intrathoracic lymph nodes
C84.63	Anaplastic large cell lymphoma, ALK-positive, intra-abdominal lymph nodes
C84.64	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of axilla and upper limb
C84.65	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of inguinal region and lower limb
C84.66	Anaplastic large cell lymphoma, ALK-positive, intrapelvic lymph nodes

ICD-10	ICD-10 Description
C84.67	Anaplastic large cell lymphoma, ALK-positive, spleen
C84.68	Anaplastic large cell lymphoma, ALK-positive, lymph nodes of multiple sites
C84.69	Anaplastic large cell lymphoma, ALK-positive, extranodal and solid organ sites
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC