Xalkori® (crizotinib)
(Oral)

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I. Length of Authorization

Coverage is provided for 6 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 250 mg capsules: 120 capsules per 30 days (4 capsules per day)
- Xalkori 20 mg pellets: 120 pellets per 30 days (4 pellets per day)
- Xalkori 50 mg pellets: 120 pellets per 30 days (4 pellets per day)
- Xalkori 150 mg pellets: 180 pellets per 30 days (6 pellets per day)

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

- NSCLC, Histiocytic Neoplasms, Uterine Sarcoma & Cutaneous Melanoma: 500 mg per day
- ALCL & IMT: 1,000 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 [1,2]

- Used as a single agent, unless otherwise specified; **AND**
- Patient does not have congenital long QT syndrome; **AND**
- Patient does not have diagnosis of drug-related interstitial lung disease/pneumonitis; **AND**

- Patient will be assessed for visual symptoms at onset and throughout therapy *(Note: Pediatric and AYA patients with a diagnosis of ALCL or IMT should receive a full ophthalmological exam at baseline and periodically throughout treatment)*; **AND**
- Patient will avoid concomitant use with all of the following, or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented:
  - Coadministration with strong or moderate CYP3A inhibitors (e.g., ketoconazole, clarithromycin, grapefruit juice, aprepitant, diltiazem, etc.); **AND**
  - Coadministration with drugs that prolong the QT-interval (e.g., fluoroquinolone or macrolide antibiotics, venlafaxine, fluoxetine, quetiapine, ziprasidone, sumatriptan, zolmitriptan, etc.); **AND**
  - Coadministration with drugs that cause bradycardia (e.g., beta-blockers, non-dihydropyridine calcium channel blockers, clonidine, digoxin, etc.); **AND**
- Patient will avoid concomitant use with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**

Non-Small Cell Lung Cancer (NSCLC) † ‡ Φ [1,2,11,16]

- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence 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❖; **AND**
    - Used as first line therapy; **OR**
    - Used as continuation of therapy following disease progression on first-line crizotinib (*excluding use in symptomatic brain lesions or symptomatic systemic disease with multiple lesions*) ‡; **OR**
  - Patient has ROS1 rearrangement positive disease as detected by an FDA-approved or CLIA-compliant test❖; **AND**
    - Used as first line therapy; **OR**
    - Used as continuation of therapy following disease progression on first-line crizotinib if progression is asymptomatic or limited symptomatic systemic progression ‡; **OR**
  - Patient has MET exon 14 skipping mutation positive tumors as detected by an FDA-approved or CLIA-compliant test❖; **AND**
    - Used as first line therapy; **OR**
    - Used as subsequent therapy following progression on first-line systemic therapy with a non-MET exon 14 skipping mutation-targeted regimen; **OR**
  - Patient has disease with high-level MET amplification* (*metastatic disease only*); **AND**
    - Used as single agent; **OR**
    - Used in combination with osimertinib in patients with EGFR mutant NSCLC

** The definition of high-level MET amplification is evolving and may differ according to the assay used for testing. For NGS-based results, a copy number greater than 10 is consistent with high-level MET amplification.*

Inflammatory Myofibroblastic Tumor (IMT) † Φ [1,2,4,9]

- 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❖

Histiocytic Neoplasms ‡ [2]

- Patient has anaplastic lymphoma kinase (ALK) positive disease as detected by an FDA-approved or CLIA-compliant test❖; **AND**
- Patient has one of the following sub-types of disease:
  - Erdheim-Chester Disease; **AND**
    - Patient has symptomatic disease; **OR**
    - Used for relapsed or refractory disease; **OR**
  - Rosai-Dorfman Disease; **AND**
    - Patient has symptomatic disease that is multifocal or unresectable unifocal; **OR**
    - Used for relapsed or refractory disease; **OR**
  - Langerhans Cell Histiocytosis (LCH); **AND**
    - Used for multisystem disease with symptomatic or impending organ dysfunction or critical organ involvement (ie, CNS, liver, spleen); **OR**
    - Used for single-system lung LCH; **OR**
    - Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate; **OR**
    - Patient has CNS lesions; **OR**
    - Used for relapsed or refractory disease

Anaplastic Large Cell Lymphoma (ALCL) † ‡ Φ [1-3]

- 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 initial palliative intent therapy OR subsequent therapy for relapsed or refractory disease

Uterine Sarcoma (Uterine Neoplasms) ‡ [2,9]

- Patient has anaplastic lymphoma kinase (ALK) positive disease as detected by an FDA-approved or CLIA-compliant test❖; **AND**
- Patient has inflammatory myofibroblastic tumor (IMT); **AND**
- Patient has advanced, recurrent/metastatic, or inoperable disease

Cutaneous Melanoma ‡ [2, 15]

- Patient has ROS1 gene fusion-positive disease as detected by an FDA-approved or CLIA-compliant test❖; **AND**
- Patient has metastatic or unresectable disease; **AND**
- Used as subsequent therapy for disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy

❖ *If confirmed using an FDA approved assay – http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage may be renewed based upon the following criteria:

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

****Non-Small Cell Lung Cancer (continuation of therapy following disease progression)**

- *Refer to Section III for criteria*

V. Dosage/Administration [1,9]

Indication	Dose
Non-Small Cell Lung Cancer, Histiocytic Neoplasms, Cutaneous Melanoma, Uterine Sarcoma	250 mg capsules orally twice daily until disease progression or unacceptable toxicity. ***Note:*** *For adults who cannot swallow capsules, the recommended dosage of XALKORI pellets is 250 mg (2 x 50 mg + 1 x 150 mg) orally, twice daily.*
Anaplastic Large Cell Lymphoma	280 mg/m^2 orally twice daily until disease progression or unacceptable toxicity. Δ *(See the dosing table below for the appropriate formulation to administer).*

Inflammatory Myofibroblastic Tumor [IMT]	**Adults** 250 mg capsules orally twice daily until disease progression or unacceptable toxicity. ***Note:*** *For adults who cannot swallow capsules, the recommended dosage of XALKORI pellets is 250 mg (2 x 50 mg + 1 x 150 mg) orally, twice daily.* **Pediatric Patients Δ** 280 mg/m² capsules OR pellets orally twice daily until disease progression or unacceptable toxicity *(See the dosing table below for the appropriate formulation to administer).*

Δ Recommended Dose for Pediatric and Young Adult Patients with ALCL or for Pediatric Patients with IMT

Body Surface Area (BSA)	Recommended Xalkori Dosage to Achieve 280 mg/m2 Twice Daily	Dose Strength Combinations of Xalkori **PELLETS§**	Dose Strength Combinations of Xalkori **CAPSULES**
0.38 to 0.46 m^2	120 mg twice daily	1 x 20 mg + 2 x 50 mg	N/A
0.47 to 0.51 m^2	140 mg twice daily	2 x 20 mg + 2 x 50 mg	N/A
0.52 to 0.61 m^2	150 mg twice daily	1 x 150 mg	N/A
0.62 to 0.80 m^2	200 mg twice daily	1 x 50 mg + 1 x 150 mg	N/A
0.81 to 0.97 m^2	250 mg twice daily	2 x 50 mg + 1 x 150 mg	N/A
0.98 to 1.16 m^2	300 mg twice daily	2 x 150 mg	N/A
1.17 to 1.33 m^2	350 mg twice daily	1 x 50 mg + 2 x 150 mg	N/A
1.34 to 1.51 m^2	400 mg twice daily	2 x 50 mg + 2 x 150 mg	2 x 200 mg
1.52 to 1.69 m2	450 mg twice daily	3 x 150 mg	1 x 200 mg + 1 x 250 mg
1.7 m2 or greater	500 mg twice daily	1 x 50 mg + 3 x 150 mg	2 x 250 mg

§ *No more than 4 oral pellet shells are to be used for a single dose.*

Note: Provide standard antiemetic and antidiarrheal agents for gastrointestinal toxicities. Antiemetics are recommended prior to and during treatment with Xalkori to prevent nausea and vomiting.

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC(s):

- Xalkori 200 mg capsule – 00069-8141-xx
- Xalkori 250 mg capsule – 00069-8140-xx
- Xalkori 20 mg pellets – 00069-0251-xx
- Xalkori 50 mg pellets – 00069-0507-xx
- Xalkori 150 mg pellets – 00069-1500-xx

VII. References

1. Xalkori [package insert]. New York, NY; Pfizer, Inc; September 2023. Accessed April 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Crizotinib. National Comprehensive Cancer Network, 2024. 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 April 2024.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) T-Cell Lymphomas. Version 3.2024. National Comprehensive Cancer Network, 2024. 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 April 2024.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Soft Tissue Sarcoma. Version 3.2023. National Comprehensive Cancer Network, 2024. 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 April 2024.
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11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Non-Small Cell Lung Cancer. Version 4.2024. National Comprehensive Cancer Network, 2024. 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 April 2024.
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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

ICD-10	ICD-10 Description
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
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthu
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified

ICD-10	ICD-10 Description
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
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part 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
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
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.5	Multifocal and unisystemic Langerhans-cell histiocytosis
C96.6	Unifocal Langerhans-cell histiocytosis
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D76.3	Other histiocytosis syndromes
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.831	Personal history of malignant neoplasm of soft tissue

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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