

Zykadia® (ceritinib) (Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

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

- Zykadia 150 mg capsules or tablets: 5 capsules or tablets per day

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

Anaplastic Large Cell Lymphoma, NSCLC (ROS1 positive disease only)

- 750 mg daily

All other indications

- 450 mg daily

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria ^{1,2}

- Used as a single agent; **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 CYP3A inhibitors (e.g. ketoconazole, clarithromycin, ritonavir, 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 all of the following:
 - Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort etc.); **AND**
 - Coadministration with grapefruit and grapefruit juice; **AND**

Non-Small Cell Lung Cancer † ‡ ⬢^{1,2}

- Patient has 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 test or CLIA-compliant test⬢; **AND**
 - Used as first-line therapy; **OR**
 - Patient is intolerant to crizotinib; **OR**
 - Used as subsequent therapy following disease progression on first-line therapy with crizotinib; **OR**
 - Used as continuation of therapy following disease progression on first-line ceritinib (*excluding use in cases of symptomatic systemic disease with multiple lesions*) ‡; **OR**
 - Patient has ROS1 rearrangement positive disease as detected by an FDA-approved test or CLIA-compliant test⬢; **AND**
 - Used as first-line therapy; **OR**
 - Used as continuation of therapy following disease progression on first-line ceritinib (*excluding use in cases of symptomatic systemic disease with multiple lesions*) ‡

Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT) ‡²

- Patient has ALK-positive disease as detected by an FDA-approved test or CLIA-compliant test⬢

Central Nervous System (CNS) Cancer ‡²

- Used for the treatment of brain metastases in patients with ALK rearrangement-positive non-small cell lung cancer as detected by an FDA-approved test or CLIA-compliant test⬢; **AND**
 - Used as initial treatment in patients with small asymptomatic brain metastases; **OR**
 - Used for relapsed limited brain metastases with either stable systemic disease or reasonable systemic treatment options; **OR**
 - Patient has recurrent limited brain metastases; **OR**
 - Used for recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options

Histiocytic Neoplasms – Erdheim-Chester Disease ‡^{2,6}

- Patient has ALK-positive disease as detected by an FDA-approved test or CLIA-compliant test❖; **AND**
 - Patient has symptomatic disease; **OR**
 - Used for relapsed or refractory disease

Uterine Neoplasms – Uterine Sarcoma ‡^{2,3}

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

Anaplastic Large Cell Lymphoma (ALCL) ‡²

- 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

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

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

IV. Renewal Criteria¹

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, bradycardia, hyperglycemia, QT interval prolongation, interstitial lung disease (ILD)/pneumonitis, severe gastrointestinal adverse reactions, pancreatitis, etc.; **AND**
- Disease response with treatment as defined by stabilization or 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^{1,5,7,8}

Indication	Dose
Anaplastic Large Cell Lymphoma,	750 mg orally once daily until disease progression or unacceptable toxicity.

NSCLC (ROS1 positive disease only)	
All Other Indications	450 mg orally once daily until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCP/CS Code(s):

- J8999 – Prescription drug, oral, chemotherapeutic, Not Otherwise Specified
- C9399 – Unclassified drugs or biologicals

NDC:

- Zykadia 150 mg capsules*: 00078-0640-xx
- Zykadia 150 mg tablet: 00078-0694-xx

*No longer commercially available

VII. References

1. Zykadia [package insert]. East Hanover, NJ: Novartis, October 2021. Accessed April 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for ceritinib. 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. Shaw AT, Kim DW, Mehra R, et al. Ceritinib in ALK-rearranged non-small-cell lung cancer. *N Engl J Med*. 2014 Mar 27;370(13):1189-97. doi: 10.1056/NEJMoa1311107.
4. Soria JC, Tan DSW, Chiari R, et al. First-line ceritinib versus platinum-based chemotherapy in advanced ALK-rearranged non-small-cell lung cancer (ASCEND-4): a randomised, open-label, phase 3 study. *Lancet*. 2017 Mar 4;389(10072):917-929. doi: 10.1016/S0140-6736(17)30123-X.
5. Kim DW, Mehra R, Tan DSW, et al. Activity and safety of ceritinib in patients with ALK-rearranged non-small-cell lung cancer (ASCEND-1): updated results from the multicentre, open-label, phase 1 trial. *Lancet Oncol*. 2016;17(4):452–463. doi:10.1016/S1470-2045(15)00614-2.
6. Kemps PG, Picarsic J, Durham BH, et al. ALK-positive histiocytosis: a new clinicopathologic spectrum highlighting neurologic involvement and responses to ALK inhibition. *Blood* 2022;139:256-280. <https://doi.org/10.1182/blood.2021013338>.
7. Richly H, Kim TM, Schuler M, et al. Ceritinib in patients with advanced anaplastic lymphoma kinase-rearranged anaplastic large-cell lymphoma. *Blood* 2015;126:1257-1258.
8. Lim SM, et al. Open-label, multicenter, phase II study of ceritinib in patients with nonsmall-cell lung cancer harboring ROS1 rearrangement. *J Clin Oncol* 2017;35:2613- 2618.

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
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
C79.31	Secondary malignant neoplasm of brain
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

ICD-10	ICD-10 Description
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
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)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
15	KY, OH	CGS Administrators, LLC