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: 3 capsules or tablets per day

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

- 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; **AND**

- 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 † Φ [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's disease is anaplastic lymphoma kinase (ALK)-positive 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, except in cases of symptomatic systemic disease with limited metastases; **OR**
    - Used as continuation of therapy following disease progression on first-line ceritinib, except in cases of symptomatic systemic disease with multiple lesions; **OR**
  - Patient's disease is ROS-1 positive 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 if progression is asymptomatic or limited symptomatic systemic metastases

Soft Tissue Sarcoma (Inflammatory Myofibroblastic Tumor [IMT]) ‡ [2]

- Patient's disease is ALK-positive 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

§ *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 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**
- 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; **OR**

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

- *Refer to Section III for criteria*

V. Dosage/Administration [1,5]

Indication	Dose
All Indications	450 mg orally once daily until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J8999: Prescription drug, oral, chemotherapeutic, Not Otherwise Specified
- C9399: Unclassified drugs or biologicals (Hospital Outpatient use only)

NDC(s):

- Zykadia 150 mg capsule: 00078-0640-xx
- Zykadia 150 mg tablet: 00078-0694-xx

VII. References

1. Zykadia [package insert]. East Hanover, NJ: Novartis, October 2021. Accessed April 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for ceritinib. National Comprehensive Cancer Network, 2022. 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 2022.
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.

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
C79.31	Secondary malignant neoplasm of brain
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 Article (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/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