Effective Date **2/1/2023**
Next Review Date **2/1/2024**

Prior Authorization
Oncology – Zykadia® (ceritinib capsules and tablets)

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Product Identifier(s)

44412

INSTRUCTIONS FOR USE
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National Formulary Medical Necessity

Cigna covers ceritinib (Zykadia®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

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

FDA Indication(s)

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

Other Uses with Supportive Evidence

2. **Erdheim-Chester Disease.** Approve for 1 year if the individual meets the following criteria (A and B):
   A) Individual is ≥ 18 years of age; AND
   B) Individual has anaplastic lymphoma kinase (*ALK*) rearrangement/fusion-positive disease.

3. **Inflammatory Myofibroblastic Tumor.** Approve for 1 year if the individuals meets the following criteria (A, B, and C):
   A) Individual is ≥ 18 years of age; AND
   B) Individual has anaplastic lymphoma kinase (*ALK*)-positive disease; AND
   C) Individual meets one of the following criteria (i or ii):
      i. Individual has advanced, recurrent, or metastatic disease; OR
      ii. The tumor is inoperable.

4. **Non-Small Cell Lung Cancer with *ROS1* Rearrangement.** Approve for 1 year if the individual meets the following criteria (A, B, and C):
   A) Individual is ≥ 18 years of age; AND
   B) Individual has advanced or metastatic disease; AND
   C) Individual has *ROS1* rearrangement-positive disease.

Conditions Not Covered

Ceritinib (Zykadia®) are considered experimental, investigational or unproven for ANY other use.

Background

Overview
Zykadia, a kinase inhibitor, is indicated for the treatment of adults with metastatic **non-small cell lung cancer** (NSCLC) whose tumors are anaplastic lymphoma kinase (*ALK*)-positive as detected by an FDA-approved test.[1]

Guidelines
Zykadia is addressed in National Comprehensive Cancer Network (NCCN) guidelines:[2-5]

- **Histiocytic Neoplasms:** Guidelines (version 1.2022 – May 20, 2022) recommend Zykadia as a "useful in certain circumstances" treatment option for *ALK*-positive Erdheim-Chester Disease (category 2A).[3]
- **NSCLC:** Guidelines (version 1.2023 – December 22, 2023) recommend testing for biomarkers (e.g., *ALK* rearrangement, *ROS* proto-oncogene 1 (*ROS1)* gene rearrangement) in eligible patients with NSCLC.[4]
  - *ALK* rearrangement-positive NSCLC: If *ALK* rearrangement is discovered prior to first-line systemic therapy, Zykadia is an "other recommended therapy" (category 1). If *ALK* rearrangement is discovered during first-line systemic therapy, options are to complete the planned systemic therapy (including maintenance therapy) or to interrupt the systemic therapy and treat with Zykadia (category 2A) or another *ALK* inhibitor. NCCN recommendations for patients with disease progression often include continuing the first-line targeted therapy, depending on type of progression.
  - *ROS1* rearrangement-positive NSCLC: If *ROS1* rearrangement is discovered prior to first-line systemic therapy, Zykadia is an "other recommended" first-line treatment option (category 2A). If *ROS1* rearrangement is discovered during first-line systemic therapy, options are to complete the planned systemic therapy (including maintenance therapy) or interrupt and treat with Zykadia (category 2A). For patients who progress on treatment, if they are asymptomatic, they may continue to receive the treatment they were previously receiving (including Zykadia) or switch to Lorbrena® (lorlatinib tablets). There are different recommendations for patients who are symptomatic, depending on type of progression.
- **Inflammatory Myofibroblastic Tumor (IMT):** NCCN Soft Tissue Sarcoma guidelines (version 2.2022 – May 17, 2022) and NCCN Uterine Neoplasms guidelines (version 1.2023 – December 22, 2022) recommend Zykadia as a treatment option for IMT with *ALK* translocation.[5,6]

References

1. Zykadia® capsules and tablets [prescribing information]. East Hanover, NJ: Novartis; October 2021.
2. The NCCN Drugs & Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 5, 2022. Search terms: ceritinib.
3. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2022 – May 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 7, 2022.
4. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – December 22, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 9, 2023.
5. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 2.2022 – May 17, 2022). ©2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 5, 2022.
6. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2023 – December 22, 2022) © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 9, 2023.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	**Erdheim-Chester Disease.** This new condition of approval was added to the policy. **Inflammatory Myofibroblastic Tumor.** The condition name was changed to as listed; previously, the condition was titled Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT). **Non-Small Cell Lung Cancer with *ROS1* Rearrangement.** The criterion "Patient is receiving Zykadia as first-line treatment" was removed.	07/13/2022
Selected Revision	**Inflammatory Myofibroblastic Tumor:** The requirement that the disease is advanced, recurrent, or metastatic, or the tumor is inoperable was added.	01/11/2023