PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Lorbrena Prior Authorization Policy
- Lorbrena® (lorlatinib tablets – Pfizer)

REVIEW DATE: 12/11/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

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

GUIDELINES

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

- **B-Cell Lymphomas:** Guidelines (version 3.2024 – August 26, 2024) recommend Lorbrena (category 2A) for relapsed or refractory *ALK*-positive large B-cell lymphomas.[7]
- **Histiocytic Neoplasms:** Guidelines (version 1.2023 – August 11, 2023) recommend Lorbrena as a "useful in certain circumstances" treatment option for *ALK*-positive Erdheim-Chester disease (category 2A).[3]
- **Inflammatory Myofibroblastic Tumor (IMT):** NCCN Soft Tissue Sarcoma guidelines (version 2.2023 – April 25, 2023) and NCCN Uterine Neoplasms guidelines (version 1.2023 – December 22, 2022) recommend Lorbrena as a treatment option for IMT with *ALK* translocation.[5,6]

- **NSCLC:** Guidelines (version 11.2024 – October 15, 2024) 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, Lorbrena is a "Preferred" first-line treatment option (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 Lorbrena ("Preferred", category 2A) or another ALK inhibitor. Lorbrena is also recommended for patients who progress on other *ALK* inhibitors (category 2A). A footnote mentions that Lorbrena is an option for resistant mutations, such as ALK G1202R and L1196M (except compound L1196M/G1202R).
  - *ROS* proto-oncogene 1 *(ROS1)* rearrangement-positive NSCLC: Lorbrena is a recommended subsequent therapy (category 2A) for patients who progress on Zykadia® (ceritinib capsules and tablets), Xalkori® (crizotinib capsules), or Rozlytrek™ (entrectinib capsules). Lorbrena is not a recommended first-line treatment option for *ROS1* rearrangement-positive NSCLC.
- **Pediatric Central Nervous System Cancers:** Guidelines (version 1.2025 – November 8, 2024) recommend Lorbrena as adjuvant therapy and for recurrent or progressive disease (category 2A for both), for *ALK*-rearrangement positive pediatric diffuse high-grade gliomas.[8]

POLICY STATEMENT

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

- **Lorbrena® (lorlatinib tablets (Pfizer)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

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

Other Uses With Supportive Evidence

2. **Erdheim-Chester Disease**. Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND

B) Patient has anaplastic lymphoma kinase (*ALK*) rearrangement/fusion-positive disease.

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

4. **Large B-Cell Lymphoma.** Approve for 1 year if the patients meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has anaplastic lymphoma kinase (*ALK*)-positive disease; AND
   C) Patient has relapsed or refractory disease.

5. **Non-Small Cell Lung Cancer – *ROS1* Rearrangement-Positive.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has advanced or metastatic disease; AND
   C) Patient has *ROS1* rearrangement-positive disease; AND
   D) Patient has tried at least one of Xalkori (crizotinib capsules), Zykadia (ceritinib capsules or tablets), or Rozlytrek (entrectinib capsules).

6. **Pediatric Diffuse High-Grade Gliomas**. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is < 18 years of age; AND
   B) The tumor is positive for anaplastic lymphoma kinase (*ALK*)-positive disease; AND
   C) Patient meets ONE of the following (i or ii):
      i. The medication is used as adjuvant therapy; OR
      ii. The medication is used for recurrent or progressive disease.

CONDITIONS NOT COVERED

- **Lorbrena® (lorlatinib tablets (Pfizer)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following; criteria will be updated as new published data are available

REFERENCES

1. Lorbrena® tablets [prescribing information]. New York, NY: Pfizer; March 2021.
2. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 6, 2024. Search term: lorlatinib.

3. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2023 – August 11, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 27, 2023.
4. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 5.2023 - November 8, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 27, 2023.
5. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 2.2023 – April 25, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 27, 2023.
6. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – September 20, 2023) © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 27, 2023.
7. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2024 – January 18, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 19, 2024.
8. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2025 – November 8, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 6, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes	11/29/2023
Annual Revision	**Large B-Cell Lymphoma:** This condition and criteria for approval was added to the policy under "Other Uses with Supportive Evidence". **Pediatric Diffuse High-Grade Gliomas:** This condition and criteria for approval was added to the policy under "Other Uses with Supportive Evidence".	12/11/2024