



## PRIOR AUTHORIZATION POLICY

- POLICY:** Oncology (Oral – Anaplastic Lymphoma Kinase [ALK]-Positive Agent) – Lorbrena Prior Authorization Policy
- Lorbrena® (lorlatinib tablets – Pfizer)

**REVIEW DATE:** 12/10/2025

### 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 WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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.<sup>1</sup>

### Guidelines

Lorbrena is addressed in National Comprehensive Cancer Network (NCCN) guidelines:<sup>2-5</sup>

- **B-Cell Lymphomas:** Guidelines (version 3.2025 – August 18, 2025) recommend Lorbrena (category 2A) for relapsed or refractory ALK-positive large B-cell lymphomas.<sup>7</sup>
- **Histiocytic Neoplasms:** Guidelines (version 2.2025 – November 21, 2025) recommend Lorbrena as a "Useful in Certain Circumstances" treatment option for ALK-positive Erdheim-Chester disease (category 2A).<sup>3</sup>

- **Inflammatory Myofibroblastic Tumor (IMT):** NCCN Soft Tissue Sarcoma guidelines (version 1.2025 – May 2, 2025) and NCCN Uterine Neoplasms guidelines (version 2.2026 – November 14, 2025) recommend Lorbrena as a treatment option for IMT with *ALK* translocation.<sup>5,6</sup> For uterine sarcoma it is recommended in advanced, recurrent/metastatic or inoperable disease.
- **NSCLC:** Guidelines (version 2.2026 – December 2, 2025) recommend testing for biomarkers (e.g., *ALK* rearrangement, *ROS* proto-oncogene 1 (*ROS1*) gene rearrangement) in eligible patients with NSCLC.<sup>4</sup>
  - *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, 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 Augtyro (repotrectinib capsules), Xalkori® (crizotinib capsules), Ibtrozi (taletrectinib 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 1.2026 – November 25, 2025) recommend Lorbrena as adjuvant therapy and for recurrent or progressive disease (category 2A for both), for *ALK*-rearrangement positive pediatric diffuse high-grade gliomas.<sup>8</sup>
- **T-Cell Lymphomas:** Guidelines (version 2.2025 – May 28, 2025) recommend Lorbrena as a treatment option for *ALK*-positive anaplastic large cell lymphoma (ALCL) as a second-line and subsequent therapy option (category 2A) for relapsed or refractory disease under “Other Recommended Regimens”.<sup>9</sup> *ALK*-positive ALCL predominantly occurs in children and young adults.<sup>10</sup>

## 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, and C):
  - 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

### Other Uses With Supportive Evidence

**2. Anaplastic Large Cell Lymphoma (ALCL).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):

- A) Patient has anaplastic lymphoma kinase (*ALK*)-positive disease; AND
- B) Patient has relapsed or refractory disease; AND
- C) The medication will be used as subsequent therapy.

**3. Erdheim-Chester Disease.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient has anaplastic lymphoma kinase (*ALK*) rearrangement/fusion-positive disease.

**4. Inflammatory Myofibroblastic Tumor.** Approve for 1 year if the patients meets ALL of the following (A, B, and C):

- A) Patient is  $\geq 18$  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.

**5. Large B-Cell Lymphoma.** Approve for 1 year if the patients meets ALL of the following (A, B, and C):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient has anaplastic lymphoma kinase (*ALK*)-positive disease; AND
- C) Patient has relapsed or refractory disease.

**6. 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  $\geq 18$  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), Augtyro (repotrectinib capsules), Ibtrozi (taletrectinib capsules), or Rozlytrek (entrectinib capsules).

**7. 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 not medically necessary for ANY other use(s). Criteria will be updated as new published data are available):**

**REFERENCES**

1. Lorbrena® tablets [prescribing information]. New York, NY: Pfizer; February 2025.
2. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 3, 2025. Search term: lorlatinib.
3. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 2.2025 – November 21, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 5, 2025.
4. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 2.2026 - December 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 5, 2025.
5. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 1.2025 – May 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 5, 2025.
6. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 2.2026 – November 14, 2025) © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 5, 2025.
7. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 3.2025 – August 18, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 5, 2025.
8. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2026 – November 25, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 5, 2025.
9. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – May 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on December 5, 2025.
10. Anaplastic Large Cell Lymphoma. Available at: <https://my.clevelandclinic.org/health/diseases/24029-anaplastic-large-cell-lymphoma>. Accessed on December 5, 2025.

**HISTORY**

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes	11/29/2023
Annual Revision	<p><b>Large B-Cell Lymphoma:</b> This condition and criteria for approval was added to the policy under “Other Uses with Supportive Evidence”.</p> <p><b>Pediatric Diffuse High-Grade Gliomas:</b> This condition and criteria for approval was added to the policy under “Other Uses with Supportive Evidence”.</p>	12/11/2024
Update	04/16/2025: The policy name was changed from “Oncology – Lorbrena PA Policy” to “Oncology (Oral – Anaplastic Lymphoma Kinase [ALK]-Positive Agent) – Lorbrena PA Policy”.	N/A

Annual Revision	<p><b>Non-Small Cell Lung Cancer – Anaplastic Lymphoma Kinase (ALK)-Positive:</b> Deleted requirement “The mutation was detected by an approved test”.</p> <p><b>Anaplastic Large Cell Lymphoma (ALCL):</b> New condition of approval and criteria was added under “Other Uses with Supportive Evidence”.</p> <p><b>Non-Small Cell Lung Cancer – ROS1 Rearrangement-Positive:</b> In reference to trial of one previous therapy, Zykadia was removed. Augtyro and Ibtrozi were added as prior therapies to try.</p>	12/10/2025
-----------------	---	------------

N/A – Not applicable.

"Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group. © 2026 The Cigna Group.