Lorbrena® (lorlatinib)
(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]:

- Lorbrena 25 mg tablets: 3 tablets per day
- Lorbrena 100 mg tablets: 1 tablet per day

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

- 100 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 therapy 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 moderate CYP3A inducers (e.g., bosentan, efavirenz, modafinil, phenobarbital, primidone, etc.); **AND**
  - Coadministration with strong CYP3A inhibitors (e.g., clarithromycin, cobicistat, nefazodone, itraconazole, ketoconazole, etc.); **AND**
  - Coadministration with fluconazole; **AND**
- Patient will avoid concomitant use with strong CYP3A inducers (e.g., apalutamide, carbamazepine, rifampin, etc.); **AND**

- Baseline electrocardiogram (ECG) has been obtained prior to initiating therapy and will be monitored periodically while on therapy; **AND**

Non-Small Cell Lung Cancer (NSCLC) † 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 has anaplastic lymphoma kinase (ALK)-positive disease as detected by an FDA-approved or CLIA-compliant test❖ †; **AND**
    - Used as first line therapy; **OR**
    - Patient is intolerant to crizotinib; **OR**
    - Used as subsequent therapy, if not previously given, following disease progression on either alectinib, brigatinib, ceritinib, or crizotinib; **OR**
    - Used as continuation of therapy following disease progression on first-line lorlatinib (*excluding use in cases of symptomatic systemic disease with multiple lesions*); **OR**
  - Patient has ROS1 rearrangement-positive disease as detected by FDA-approved or CLIA-compliant test❖ ‡; **AND**
    - Used as subsequent therapy following disease progression on crizotinib, entrectinib, or ceritinib; **AND**
    - Patient has asymptomatic progression or symptomatic systemic progression

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 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

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

- Patient has anaplastic lymphoma kinase (ALK)-positive disease as detected by an FDA-approved or CLIA-compliant test❖

Histiocytic Neoplasms – Erdheim-Chester Disease ‡ [2,6]

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

Uterine Sarcoma ‡ [2]

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

Diffuse Large B-Cell Lymphoma ‡ [2]

- Patient has anaplastic lymphoma kinase (ALK)-positive disease as detected by an FDA-approved or CLIA-compliant test❖; **AND**
- Used for relapsed or refractory large B-Cell lymphoma

❖*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 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, CNS effects (e.g., seizures, psychotic effects, and changes in mood, cognitive function, speech, mental status, and sleep, etc.), atrioventricular (AV) block, hyperlipidemia, interstitial lung disease (ILD)/pneumonitis, hypertension, hyperglycemia, etc.; **AND**
- Disease response with treatment as defined by stabilization of 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]

Indication	Dose
All Indications	100 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 *(for hospital outpatient use ONLY)*

NDC(s):

- Lorbrena 25 mg tablet: 00069-0227-xx
- Lorbrena 100 mg tablet: 00069-0231-xx

VII. References

1. Lorbrena [package insert]. New York, NY; Pfizer, April 2023. Accessed April 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for lorlatinib. National Comprehensive Cancer Network, 2023. 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 2023.
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. Solomon BJ, Besse B, Bauer TM, et al. Lorlatinib in patients with ALK-positive non-small-cell lung cancer: results from a global phase 2 study. Lancet Oncol. 2018 Dec;19(12):1654-1667. doi: 10.1016/S1470-2045(18)30649-1.
5. Shaw A, Bauer T, Marinis F, et al. First-Line Lorlatinib or Crizotinib in Advanced ALK-Positive Lung Cancer. N Engl J Med 2020; 383:2018-2029 DOI: 10.1056/NEJMoa2027187
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.

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

ICD-10	ICD-10 Description
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
C83. 30	Diffuse large B-cell lymphoma, unspecified site
C83. 31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83. 32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83. 33	Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83. 34	Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83. 35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83. 36	Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83. 37	Diffuse large B-cell lymphoma, spleen
C83. 38	Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83. 39	Diffuse large B-cell lymphoma, extranodal and solid organ sites
C83. 90	Non-follicular (diffuse) lymphoma, unspecified, unspecified site
C83. 91	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck
C83. 92	Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C83. 93	Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes
C83. 94	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb
C83. 95	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C83. 96	Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes
C83. 97	Non-follicular (diffuse) lymphoma, unspecified, spleen

ICD-10	ICD-10 Description
C83. 98	on-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites
C83. 99	Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites
C85. 20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85. 21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85. 22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85. 23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85. 24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85. 25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85. 26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85. 27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85. 28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85. 29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
D76.3	Other histiocytosis syndromes
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
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
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.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC