09-J3000-23

Original Effective Date: 3/15/19

Reviewed: 09/11/19

Revised: 10/15/19

Subject: Lorlatinib (Lorbrena)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Lorlatinib (Lorbrena), a kinase inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in 2018 for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on crizotinib, alectinib, or ceritinib.

The safety and efficacy of lorlatinib were evaluated in a non-randomized study of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) previously treated with 1 or more ALK kinase inhibitors (N=215). All patients received lorlatinib 1 mg daily.

The overall response rate (ORR) was 48% (complete response, 4%) and median duration of response was 12.5 months (95% CI, 8.4 to 23.7 months) with lorlatinib in In a subgroup of patients with CNS metastases (n=89), intracranial response rate was 60% (complete response, 21%) and median duration of response was 19.5 months (95% CI, 12.4 months to not reached). In exploratory analysis, ORR was 39%, 31%, and 46% in patients who received crizotinib and at least 1 other ALK inhibitor with or without chemotherapy (n=119), in patients who received alectinib as their only ALK inhibitor with or without chemotherapy (n=13), and in patients who received ceritinib as their only ALK inhibitor with or without chemotherapy (n=13), respectively.

National Comprehensive Cancer Network (NCCN) Guidelines for Non-Small Cell Lung Cancer (Version 7.2019) recommend lorlatinib for ALK- or ROS-positive recurrent, advanced or metastatic disease.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of lorlatinib (Lorbrena) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Non-small cell lung cancer (NSCLC)
    a. Member's disease is recurrent, advanced, or metastatic
    b. Member has a documented anaplastic lymphoma kinase (ALK) or ROS1 rearrangement – laboratory documentation must be provided
    c. Member meets **ONE** of the following:
        i. ALK-positive disease **AND** one of the following
            1. Use is following disease progression on first-line therapy with crizotinib **AND** subsequent therapy with alectinib, brigatinib, or ceritinib
            2. Use is following disease progression on first-line therapy with alectinib, brigatinib, or ceritinib
        ii. ROS1-positive disease **AND** use is following disease progression on crizotinib or ceritinib
    d. Use will be as monotherapy (without concomitant chemotherapy)
    e. Dose does not exceed 100 mg daily – dosage will be achieved using the fewest tablets possible
2. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    a. Member meets one of the following:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    b. Dose does not exceed 100 mg daily – dosage will be achieved using the fewest tablets possible

Approval duration: 6 months

Continuation of lorlatinib (Lorbrena) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of ALK-positive or ROS1-positive NSCLC, or other FDA-approved or NCCN supported diagnosis, **OR** the member has previously met all indication-specific criteria.
2. Dose does not exceed 100 mg daily – dosage will be achieved using the fewest tablets possible

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION

FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 100 mg orally once daily

Dose Adjustments

- First dose reduction: 75 mg once daily
- Second dose reduction: 50 mg once daily

Drug Availability

- Tablets: 25 mg or 100 mg

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Concomitant use with strong CYP3A inducers

Precautions/Warnings

- Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers
- Central Nervous System (CNS) Effects
- HyperlipidemiaAtrioventricular Block
- Embryo-Fetal Toxicity

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8999	Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

C33	Malignant neoplasm of trachea
C34.00-C34.92	Malignant neoplasm of bronchus or lung

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 8/28/19]. Available from: http://www.thomsonhc.com/.
4. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Non-small cell lung cancer, v. 3.2019 [cited 8/28/19]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
5. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2019 [cited 8/28/19]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [cited 8/28/19]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
7. Pfizer. Lorbrena (lorlatinib) tablet. 2018 [cited 8/28/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2b34d62d-e02a-4af3-bc0d-1571dd4ee76d/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 09/11/19.

GUIDELINE UPDATE INFORMATION:

03/15/19	New Medical Coverage Guideline.

10/15/19	Review and revision, updated position statement, description, references.