Clinical Policy Title:	lorlatinib
Policy Number:	RxA.407
Drug(s) Applied:	Lorbrena®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Lorbrena® is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lorlatinib (Lorbrena®)	ALK-positive NSCLC	100 mg orally once daily, For severe renal impairment (CrCl 15 to < 30 mL/min): 75 mg orally once daily	100 mg/day, 75 mg/day for severe renal impairment (CrCl 15 to < 30 mL/min)

Dosage Forms

- Tablets: 25 mg, 100 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all):

1. Diagnosis of recurrent, advanced or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease ALK or ROS1 positive;
5. If disease is ALK positive (a or b);
   a. As a single agent preferred first line therapy;
   b. As subsequent therapy following disease progression on Alecensa®, Alunbrig®, or Zykadia® unless contraindicated or clinically significant adverse effects are experienced;

*Prior authorization may be required for Alecensa®, Alunbrig®, and Zykadia®.

6. If disease is ROS1 positive, failure of Rozlytrek, Xalkori® or Zykadia® unless contraindicated or clinically significant adverse effects are experienced;
   *Prior authorization may be required for Rozlytrek, Xalkori® and Zykadia®.
7. Request meets one of the following (a or b):
   a. Dose does not exceed 100 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. CNS Cancer (Limited & Extensive Brain Metastases) (Off -Label) (must meet all):
1. Diagnosis of limited or extensive brain metastases in patients with ALK positive NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Used as a single-agent for treatment of relapsed/recurrent disease with either stable systemic disease or reasonable systemic treatment options;
5. Request meets one of the following (a or b)=
   a. ;Dose does not exceed 100 mg per day
   b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria approved for NSCLC and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 100 mg per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. APPENDICES

APPENDIX A: Abbreviation/Acronym Key
ALK: anaplastic lymphoma kinase
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Alecensa®(alectinib)	600 mg orally BID	1,200 mg/day
Alunbrig®(brigatinib)	90 mg orally once daily for the first 7 days; if tolerated, increase to 180 mg orally once daily	180 mg/day
Zykadia® (ceritinib)	450 mg orally once daily	450 mg/day
Xalkori® (crizotinib)	250 mg orally BID	500 mg/day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Concomitant use with strong CYP3A inducers.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers: Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating Lorbrena®.
- Central Nervous System (CNS) Effects: CNS effects include seizures, psychotic effects and changes in cognitive function, mood (including suicidal ideation), speech, mental status, and sleep. Withhold and resume Lorbrena® at same or reduced dose or permanently discontinue Lorbrena® based on severity.
- Hyperlipidemia: Initiate or increase the dose of lipid-lowering agents. Withhold and resume Lorbrena® at same or reduced dose based on severity.
- Atrioventricular Block: Withhold and resume Lorbrena® at same or reduced dose based on severity.
- Interstitial Lung Disease/Pneumonitis: Immediately withhold LORBRENA® in patients with suspected ILD/pneumonitis. Permanently discontinue Lorbrena® for treatment related ILD/pneumonitis of any severity.
- Hypertension: Monitor blood pressure after 2 weeks and then at least monthly during treatment. For severe hypertension, withhold Lorbrena®, then dose reduce or permanently discontinue.
- Hyperglycemia: Assess fasting serum glucose prior to starting Lorbrena® and regularly during treatment. If not adequately controlled with optimal medical management, withhold Lorbrena®, then consider dose reduction or permanently discontinue, based on severity.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus. Advise males and females of reproductive potential to use an effective non-hormonal method of contraception.

References

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6. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2b34d62d-e02a-4af3-bc0d-1571dd4ee76d . Accessed June 24, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Dosing information was updated. 3. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 4. References were updated.	07/14/2020	09/14/2020
Policy was reviewed: 1. Background was updated to remove tried therapies, "Lorbrena is indicated for the treatment of patients with ALK...". 2. Dosing Information was updated to include "Severe Renal Impairment(CrCl 15 to < 30 mL/min): 75 mg orally once daily". 3. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 4. Initial Approval Criteria I.A.5.a was updated to include "As a single agent preferred first line therapy…" 5. Initial Approval Criteria I.A.6 was updated to include Rozlytrek. 6. Initial Approval Criteria I.B was updated to include off-label indication, "CNS Cancer (Limited & Extensive Brain Metastases) (Off -Label)…" 7. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration. 8. Continued Therapy Criteria II.A was updated to "All Indications in Section I." 9. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is	6/24/2021	9/14/2021

currently receiving medication that has been authorized by RxAdvance…" 10. Appendix B - Therapeutic alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance… 11. Appendix B footnote was updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 12. .Appendix D was updated to include general information "Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers…" 13. References were reviewed and updated.		