Clinical Policy Title:	brigatinib
Policy Number:	RxA.012
Drug(s) Applied:	Alunbrig®
Original Policy Date:	02/07/2020
Last Review Date:	01/17/2022
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
brigatinib (Alunbrig®)	ALK-positive NSCLC	90 mg orally once daily for the first 7 days; increase to 180 mg orally once daily. **For Hepatic Impairment:** Severe hepatic impairment (Child-Pugh C): Reduce the dose of brigatinib by approximately 40% without breaking tablets (i.e., from 180 mg to 120 mg; from 120 mg to 90 mg; from 90 mg to 60 mg). **For Renal Impairment:** Severe renal impairment (CrCL 15 to 29 mL/min): Reduce the dose of brigatinib by approximately 50% without breaking tablets (i.e., from 180 mg to 90 mg; from 90 mg to 60 mg).	180 mg/day

Dosage Forms

- Tablets: 30 mg, 90 mg, 180 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 of age;
4. Disease is ALK-positive;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 180 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).*

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Central Nervous System Cancer (off-label) (must meet all)**:**
1. Diagnosis of Limited or Extensive Brain Metastases;
2. Individual has metastatic anaplastic lymphoma kinase (ALK)-positive NSCLC as detected by an approved test;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years of age;
5. Dose is within FDA maximum limit for any FDA-approved indication or 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

C. Soft Tissue Sarcoma (off-label) (must meet all)**:**
1. Diagnosis of Soft Tissue Sarcoma - Inflammatory Myofibroblastic Tumor (IMT) with ALK translocation;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years of age;
4. Prescribed as a preferred single-agent therapy for the treatment of inflammatory myofibroblastic tumor (IMT) with ALK translocation.

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 documentation supports that member is currently receiving Alunbrig® 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 180 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).*

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration

Commercial: 6 months
Medicaid: 6 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
Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.
- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- CYP3A Inhibitors: Avoid coadministration of Alunbrig® with strong or moderate CYP3A inhibitors. If coadministration of a strong or moderate CYP3A inhibitor is unavoidable, reduce the dose of Alunbrig®.
- CYP3A Inducers: Avoid coadministration of Alunbrig® with strong or moderate CYP3A inducers. If coadministration of a moderate CYP3A inducer is unavoidable, increase the dose of Alunbrig®.

References

1. Alunbrig® Prescribing Information, Lexington, MA : Takeda Pharmaceuticals America, Inc. ; September 2021. Available at: www.alunbrig.com. Accessed November 18, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 18, 2021.
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 7.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 18, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Updated references	05/2020	05/21/2020
Policy was reviewed: 1. Policy title table was updated. 2. Background and indication were updated to include updated FDA-approved indication. 3. Continued therapy criteria II.A.1 was rephrased to “Currently receiving	01/20/2021	03/09/2021

medication that has been authorized by RxAdvance…". 4. Approval duration was updated for commercial plans for initial and continued therapy approval from length of benefit to 6 months. 5. Initial and continued therapy approval criteria were updated to include terminology "**Prescribed regimen must be FDA-approved…*". 6. References were updated.		
Policy was reviewed: 1. Dosing Information, Dosing Regimen, Alunbrig: Updated to include hepatic impairment dosing information for indication ALK-positive metastatic non-small cell lung cancer (NSCLC). 2. Dosing Information, Dosing Regimen, Alunbrig: Updated to include renal impairment dosing information for indication ALK-positive metastatic non-small cell lung cancer (NSCLC). 3. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 4. Initial Approval Criteria I.B: Updated to include approval criteria for indication Central Nervous System Cancer. 5. Initial Approval Criteria I.C: Updated to include approval criteria for indication Soft Tissue Sarcoma. 6. Appendix D, General Information: Updated to include new information regarding Drug Interactions. 7. References were reviewed and updated.	11/19/2021	01/17/2022