Alunbrig® (brigatinib)
(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]:

- Alunbrig 30 mg tablets: 2 tablets per day
- Alunbrig 90 mg tablets: 1 tablet per day
- Alunbrig 180 mg tablets: 1 tablet per day
- Alunbrig initiation pack 90 mg/180 mg tablets: 1 pack per 30 days

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

- 180 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Used as a single agent; **AND**
- Patient has anaplastic lymphoma kinase (ALK) positive disease as detected by an FDA-approved or CLIA compliant test❖; **AND**
- Patient will avoid concomitant use with the following:
  - Coadministration with strong or moderate CYP3A inhibitors (e.g. ketoconazole, clarithromycin, diltiazem, fluvoxamine, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
  - Coadministration with moderate CYP3A inducers (e.g., bosentan, efavirenz, etravirine, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

- Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **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**
  - Used as first-line therapy; **OR**
  - Patient is intolerant to crizotinib; **OR**
  - Used as subsequent therapy following disease progression on first-line therapy with crizotinib; **OR**
  - Used as continuation of therapy following disease progression on first-line brigatinib (*excluding use in cases of symptomatic systemic disease with multiple lesions*)

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

Central Nervous System (CNS) Cancer ‡ [2]

- Used for the treatment of brain metastases in patients with non-small cell lung cancer; **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

Histiocytic Neoplasms – Erdheim-Chester Disease ‡ [2,9]

- Patient has symptomatic disease; **OR**
- Used for relapsed or refractory disease

Uterine Sarcoma ‡ [2,6,7]

- Patient has inflammatory myofibroblastic tumor (IMT); **AND**
- Patient has advanced, recurrent/metastatic, or inoperable disease

❖ *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 indication specific criteria as identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypertension, bradycardia, interstitial lung disease/pneumonitis, visual disturbances, creatine phosphokinase (CPK) elevation, pancreatic enzyme elevation, hepatotoxicity, severe hyperglycemia, photosensitivity, 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 [1,6-8]

Indication	Dose
All Indications	Administer 90 mg orally once daily for the first 7 days and, if tolerated, increase to 180 mg once daily. Administer until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, nos

NDC(s):

- Alunbrig 30 mg tablet: 63020-0113-xx
- Alunbrig 90 mg tablet: 63020-0090-xx
- Alunbrig 180 mg tablet: 63020-0180-xx
- Alunbrig 90 mg/7 count tablets and 180 mg/23 count tablets one-month initiation pack: 63020-0198-xx

VII. References

1. Alunbrig [package insert]. Lexington, MA; Ariad Pharmaceuticals, Inc., February 2022. Accessed April 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for brigatinib. 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. Camidge DR, Bazhenova L, Salgia R, et al. Safety and efficacy of brigatinib (AP26113) in advanced malignancies, including ALK+ non–small cell lung cancer (NSCLC). Journal of Clinical Oncology33, no. 15_suppl(May 20, 2015)8062-8062.
4. Ou SHI, Tiseo M, Camidge DR, et al. Brigatinib (BRG) in patients (pts) with crizotinib (CRZ)-refractory ALK+ non-small cell lung cancer (NSCLC) and brain metastases in the pivotal randomized phase 2 ALTA trial. Journal of Clinical Oncology 2017 35:15_suppl, e20502-e20502
5. Camidge DR, Kim DW, Tiseo M, et al. Exploratory Analysis of Brigatinib Activity in Patients With Anaplastic Lymphoma Kinase-Positive Non-Small-Cell Lung Cancer and Brain Metastases in Two Clinical Trials. Clin Oncol. 2018 Sep 10;36(26):2693-2701. doi: 10.1200/JCO.2017.77.5841. Epub 2018 May 16.
6. Camidge D, Kim H, Ahn M, et al. Brigatinib Versus Crizotinib in ALK-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2018 Nov 22;379(21):2027-2039. doi: 10.1056/NEJMoa1810171. Epub 2018 Sep 25.
7. Gettinger SN, Bazhenova LA, Langer CJ, et al. Activity and safety of brigatinib in ALK -rearranged non-small-cell lung cancer and other malignancies: a single-arm, open-label, phase 1/2 trial. Lancet Oncol. Vol. 17(12):1683-1696. DOI: 10.1016/S1470-2045(16)30392-8.
8. Kim DW, Tiseo M, Ahn MJ, et al. Brigatinib in Patients With Crizotinib-Refractory Anaplastic Lymphoma Kinase-Positive Non-Small-Cell Lung Cancer: A Randomized, Multicenter Phase II Trial. J Clin Oncol. 2017 Aug 1;35(22):2490-2498. doi: 10.1200/JCO.2016.71.5904.
9. 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

ICD-10	ICD-10 Description
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
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
C54.3	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
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 (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
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.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC