CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Brigatinib (Alunbrig®)

Version: 1.0

EFFECTIVE DATE: 3/1/2025

NantHealth® | Eviti®

Please note the following:

Brigatinib (Alunbrig®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Brigatinib (Alunbrig): Discussion

Brigatinib is a tyrosine kinase inhibitor (TKI) with in vitro activity at clinically achievable concentrations against multiple kinases including ALK, ROS1, insulin-like growth factor-1 receptor (IGF-1R), and FLT-3 as well as EGFR deletion and point mutations. Brigatinib inhibited autophosphorylation of ALK and ALK-mediated phosphorylation of the downstream signaling proteins STAT3, AKT, ERK1/2, and S6 in in vitro and in vivo assays.[1]

Brigatinib is a second-generation ALK inhibitor designed to overcome resistance to crizotinib. It targets a broad range of ALK rearrangements in patients with ALK-positive non-small cell lung cancer (NSCLC). It also works against epidermal growth factor receptor (EGFR)-Del (E746-A750), ROS1-L2026M, FLT3-F691L, and FLT3-D835Y mutations.[1,2]

Brigatinib is associated with adverse reactions including interstitial lung disease, pneumonitis, hypertension, bradycardia, visual disturbance, creatine phosphokinase (CPK) elevation, pancreatic enzymes elevation, hepatotoxicity, hyperglycemia, photosensitivity, embryo-fetal toxicity, diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting, and dyspnea.

Brigatinib is approved by the Food and Drug Administration (FDA) for non-small cell lung cancer.[1]

The National Comprehensive Cancer Network (NCCN) endorses brigatinib for the following cancer types: central nervous system, histiocytic neoplasms, non-small cell lung, soft tissue, T-cell lymphomas, and uterine.[3,4,5,6,7,8]

Brigatinib: Definitions

- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.

- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

Brigatinib: Policy

Note: Coverage of brigatinib will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Brigatinib will be considered for coverage when the following criteria are met:

Central Nervous System Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

Limited Brain Metastases

For **NCCN** required criteria coverage:

3. Single-agent treatment in ALK rearrangement-positive non-small cell lung cancer for one of the following:
   a) Initial treatment in select cases (e.g., patients with small asymptomatic brain metastases)
   b) Recurrent brain metastases
   c) Relapsed disease with either stable systemic disease or reasonable systemic treatment options; OR

Extensive Brain Metastases

For **NCCN** required criteria coverage:

4. Single-agent treatment in ALK rearrangement-positive non-small cell lung cancer for one of the following:
   a) Primary treatment in select cases (e.g., small asymptomatic brain metastases)
   b) Recurrent disease with stable systemic disease or reasonable systemic treatment options.[3]

Histiocytic Neoplasms - Erdheim-Chester Disease

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. First-line or subsequent therapy for anaplastic lymphoma kinase (ALK)-fusion target as a single agent for one of the following:
   a) Symptomatic disease
   b) Relapsed/refractory disease.[4]

Non-Small Cell Lung Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

4. Anaplastic lymphoma kinase (ALK)-positive metastatic disease[1]; OR

For **NCCN** required criteria coverage:

5. Single agent therapy for ALK rearrangement positive recurrent, advanced, or metastatic disease for one of the following:
   a) First-line therapy
   b) Intolerance to crizotinib
   c) Following disease progression on first-line therapy with brigatinib, as continuation of therapy except in cases of symptomatic systemic disease with multiple lesions
   d) Subsequent therapy following disease progression on first-line therapy with crizotinib.[5]

Soft Tissue Sarcoma - Inflammatory Myofibroblastic Tumor (IMT) with ALK Translocation

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent therapy.[6]

T-Cell Lymphomas - Peripheral T-Cell Lymphoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Initial palliative intent therapy or second-line and subsequent therapy as a single agent for relapsed/refractory ALK-positive anaplastic large cell lymphoma (ALCL).[7]

Uterine Neoplasms - Uterine Sarcoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. First-line therapy for advanced, recurrent/metastatic, or inoperable disease (or second-line or subsequent therapy as clinically appropriate if not used previously) as a single agent for inflammatory myofibroblastic tumor (IMT) with ALK translocation for one of the following:
   a) Primary treatment of known or suspected extrauterine disease, diagnosed by biopsy or myomectomy
   b) Primary treatment of disease that is not suitable for primary surgery (disease is not amenable to resection or the patient is not suitable for surgery based on comorbidities)
   c) Additional therapy following total hysterectomy ± bilateral salpingo-oophorectomy (TH ± BSO) for stage II-III IMT with ALK translocation
   d) Additional therapy following TH ± BSO for stage IV IMT with ALK translocation
   e) Preoperatively or postoperatively for recurrent disease with resectable isolated metastases
   f) Recurrent disease with unresectable isolated metastases or disseminated disease
   g) Radiologically isolated vaginal/pelvic recurrence if no prior radiation therapy (RT) was, given in combination with RT
   h) Radiologically isolated vaginal/pelvic recurrence if prior RT was given with or without RT.[8]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Brigatinib: References

1. Brigatinib (Alunbrig) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208772s013lbl.pdf. Accessed March 5, 2025.
2. Xing et al. Efficacy and safety of brigatinib in ALK-positive non-small cell lung cancer treatment: A systematic review and meta-analysis. https://pmc.ncbi.nlm.nih.gov/articles/PMC9669367/. Accessed March 5, 2025.
3. National Comprehensive Cancer Network. Central Nervous System Cancers. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed March 5, 2025.
4. National Comprehensive Cancer Network. Histiocytic Neoplasms. https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed March 5, 2025.
5. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed March 5, 2025.
6. National Comprehensive Cancer Network. Soft Tissue Sarcoma. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed March 5, 2025.
7. National Comprehensive Cancer Network. T-Cell Lymphomas. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed March 5, 2025.

8. National Comprehensive Cancer Network. Uterine Neoplasms. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed March 5, 2025.

Brigatinib: Coding (CPT®, ICD-10, and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C34.90	Non-small cell lung cancer
C49.9	Soft tissue neoplasms
C55.0	Uterine neoplasms
C72.9	Central nervous system cancer
C79.31	Limited brain metastases
C79.32	Extensive brain metastases
C84.90	T-cell lymphomas
E88.89	Erdheim-Chester syndrome
J9034	Brigatinib

Brigatinib: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	3/1/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	3/20/2025
6	Revision Changes:	