Regence Oregon and Utah | Regence Idaho and select counties of Washington

Independent licensees of the Blue Cross and Blue Shield Association

Medication Policy Manual	**Policy No:** dru506
Topic: Alunbrig™, brigatinib	**Date of Origin:** August 11, 2017
Committee Approval Date: August 11, 2017	**Next Review Date:** August 2018
Effective Date: August 11, 2017	

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Brigatinib (Alunbrig™) is an oral targeted therapy for the treatment of patients with anaplastic lymphoma kinase (ALK) positive (ALK-positive) non-small cell lung cancer (NSCLC). It is given following disease progression on front-line targeted therapy.

Policy/Criteria

I. Most contracts require prior authorization approval of brigatinib (Alunbrig) prior to coverage. Brigatinib (Alunbrig) may be considered medically necessary when criteria A, B, and C, below are met.

A. A diagnosis of ALK-positive, metastatic NSCLC

AND

B. Progression of disease on or intolerance to crizotinib (Xalkori®)

AND

C. Brigatinib (Alunbrig) will be used as monotherapy

II. Administration, Quantity Limitations, and Authorization Period

A. Regence Pharmacy Services considers brigatinib (Alunbrig) to be a self-administered medication.

B. When prior authorization is approved, brigatinib (Alunbrig) may be authorized in quantities of up to 180 mg daily.

C. Authorization shall be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Brigatinib (Alunbrig) is considered investigational when used as a first-line treatment for ALK-positive, metastatic NSCLC.

IV. Brigatinib (Alunbrig) is considered investigational when used for all other conditions.

Position Statement

Summary

- Brigatinib (Alunbrig), a tyrosine kinase inhibitor (TKI) that blocks the ALK pathway, is approved for the treatment of ALK-positive metastatic NSCLC when there is intolerance to, or progression of disease on crizotinib (Xalkori).
- The intent of this policy is to provide coverage for brigatinib (Alunbrig) for its FDA-labeled indication.
- Brigatinib (Alunbrig) was approved via the FDA's Accelerated approval pathway. Conditional approval is based on tumor response rates from a single, on-going, phase 2 trial. There is currently no evidence that it provides any clinically meaningful benefit, such as improved survival, quality of life, or symptom control. [1]
- Brigatinib (Alunbrig) was studied in patients with metastatic ALK-positive NSCLC that progressed while taking crizotinib (Xalkori). [2]
- The NCCN NSCLC treatment guideline lists brigatinib (Alunbrig) among alectinib (Alecensa®) and ceritinib (Zykadia®) as category 2A options following progression on front-line therapy. [3]

- Adverse effects reported with brigatinib (Alunbrig) are generally similar to other ALK inhibitors and include nausea, diarrhea, fatigue, cough and headache. Unique adverse events to brigatinib (Alunbrig) include early-onset pulmonary symptoms and hypertension. [1]
- The approved dosing for brigatinib (Alunbrig) is 180 mg (2 tablets) orally once daily until disease progression. [1]
- There is interest in using brigatinib (Alunbrig) earlier in NSCLC treatment (first-line); however, there is currently no peer-reviewed evidence in this setting.

Clinical Efficacy

- Approval of brigatinib (Alunbrig) was based on an ongoing phase 2, open-label, non-comparative study in adults with ALK-positive, locally advanced or metastatic, NSCLC who had progressed on crizotinib. [2]
- The primary endpoint was objective response rate (ORR). ORR is not a validated surrogate endpoint. It has not been shown to accurately predict any clinically relevant benefit in NSCLC.
- The study included two arms, but was not designed for statistical comparison between groups. One arm evaluated brigatinib at a dose of 90 mg/day, while the other evaluated brigatinib at a dose of 180 mg/day with a seven-day lead-in at 90 mg/day.
- The reported ORR was 54% in the 180 mg/day arm (FDA-labeled dose) with a duration of response (DOR) of 11.1 months.
- To date, it is unknown if the use of brigatinib (Alunbrig) in this setting improves survival, symptom control, or quality of life.
- Brigatinib (Alunbrig) has not been directly compared to any other ALK inhibitor for NSCLC.

Investigational Uses

- There are no published clinical trials evaluating the safety or efficacy of generic (Brand) for the treatment of conditions outside of ALK-positive NSCLC.
- Although brigatinib (Alunbrig) is being studied for use as a front-line agent for ALK-positive NSCLC, there is currently no published evidence supporting its safety or efficacy in this setting. [4]

Regence Pharmacy Services performs independent analyses of oncology medications. The Regence Pharmacy Services analysis and coverage policy may differ from NCCN clinical practice guidelines.

Cross References
Molecular Analysis for Targeted Therapy of NSCLC, Medical Policy Manual, Genetic Testing Policy No. 56
Alecensa®, alectinib, Medication Policy Manual No. dru450
Alimta®, pemetrexed, Medication Policy Manual No. dru213
Avastin®, bevacizumab, Medication Policy Manual No. dru215
Cyramza®, ramucirumab, Medication Policy Manual No. dru355
Gilotrif®, afatinib, Medication Policy Manual No. dru317
Iressa®, gefitinib, Medication Policy Manual No. dru418
Keytruda®, pembrolizumab, Medication Policy Manual No. dru367
Opdivo®, nivolumab, Medication Policy Manual No. dru390
Portrazza™, necitumumab, Medication Policy Manual No. dru449
Tagrisso™, osimertinib, Medication Policy Manual No. dru441
Tarceva®, erlotinib, Medication Policy Manual No. dru118
Tecentriq™, atezolizumab, Medication Policy Manual No. dru463
Xalkori®, crizotinib, Medication Policy Manual No. dru265
Zykadia®, ceritinib, Medication Policy Manual No. dru354

Codes	Number	Description
HCPCS	J8999	Oral chemotherapeutic drug, not otherwise classified

References

1. ALUNBRIG™ (brigatinib) tablets, for oral use [package insert]. Cambridge, MA: ARIAD Pharmaceuticals Inc; April 2017.
2. 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. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2017 May 05:JCO2016715904. PMID: 28475456
3. NCCN Clinical Practice Guidelines in Oncology™. Non-small cell lung cancer v.6.2017 [cited 5/17/2017]; Available from: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
4. ARIAD Announces Initiation of Randomized, First-Line Phase 3 Trial of Brigatinib in Treatment of ALK-Positive Non-Small Cell Lung Cancer. [cited 5/25/17]; Available from: http://investor.ariad.com/phoenix.zhtml?c=118422&p=irol-newsArticle&ID=2155832

Revision History

Revision Date	Revision Summary
08/11/2017	New policy (effective 08/11/2017)