Alunbrig (brigatinib)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Alunbrig
- **Generic name:** Brigatinib
- **Pharmacological class:** Kinase inhibitor
- **Strength and Formulation:** 30mg, 90mg; tabs
- **Manufacturer:** Takeda Pharmaceuticals
- **How supplied:** 30mg—21,180; 90mg—7,30
- **Legal Classification:** Rx

ALUNBRIG


NDC 76189-113-18
Alunbrig™
(brigatinib) tablets
30 mg
Rx Only
180 Tablets

Indications

- Treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic **non-small cell lung cancer (NSCLC)** who have progressed or are intolerant to crizotinib

Dosage & Administration

- Swallow whole
- Initially 90mg once daily for first 7 days; if tolerated increase to 180mg once daily until disease progression or unacceptable toxicity
- Dose modifications/dose reductions: see full labeling

Considerations for Special Populations

- **Pregnancy:** Avoid
- **Nursing mothers:** Not recommended (during and for 1 week after final dose)
- **Pediatric:** Not established
- **Elderly:** No clinically relevant differences in safety or efficacy
- **Hepatic or renal impairment:** Severe impairment: not studied

Warnings/Precautions

- **Monitor** for new or worsening respiratory symptoms especially during 1st week of initiation; if occurs, withhold and evaluate for interstitial lung disease (ILD)/pneumonitis
- Resume at same dose for **Grade 1** or reduced dose for **Grade 2 severity**
- **Permanently discontinue** for Grade 3/4 or recurrent Grade 1/2 ILD/pneumonitis

Warnings/Precautions

- **Monitor BP** after 2 weeks and at least monthly thereafter
- **Withhold** for Grade 3 hypertension despite optimal antihypertensive therapy; resume at reduced dose upon improvement to Grade 1 severity
- Consider **permanent discontinuation** for Grade 4 or recurrent Grade 3 hypertension

Warnings/Precautions

- **Monitor HR and BP regularly**; if symptomatic bradycardia occurs, withhold and evaluate any concomitant drugs that are known to cause bradycardia
- **Resume** at same or reduced dose after resolution; **discontinue** for life-threatening bradycardia if no contributing concomitant medication identified

Warnings/Precautions

- Withhold and evaluate for **new or worsening visual symptoms** of Grade ≥2 severity
- Resume at reduced doses upon recovery to Grade 1 or baseline; **permanently discontinue** for Grade 4 visual disturbances
- Monitor **CPK, lipase, and amylase levels** during treatment; withhold for **Grade 3/4 elevation**; resume at same or reduced dose upon recovery to Grade 1 or baseline

Warnings/Precautions

- Assess **fasting serum glucose** prior to initiation and periodically thereafter
- If not adequately controlled with optimal antihyperglycemics, withhold then consider dose reduction, or permanently discontinue based on severity

Warnings/Precautions

- Embryo-fetal toxicity
- Females of reproductive potential should use effective non-hormonal contraception during treatment and **for at least 4 months** after final dose
- Males should use effective contraception during treatment and **for at least 3 months** after final dose

Interactions

- Avoid concomitant **strong CYP3A inhibitors** (eg, boceprevir, cobicistat, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, clarithromycin, itraconazole, ketoconazole, posaconazole, voriconazole, conivaptan)
  - If unavoidable, reduce Alunbrig dose by ~50%

Interactions

- Avoid **grapefruit or grapefruit juice**
- Avoid concomitant **strong CYP3A inducers** (eg, rifampin, carbamazepine, phenytoin, St. John's wort)
- May reduce efficacy of **CYP3A substrates** (eg, hormonal contraceptives)
- Caution with antihypertensives that cause bradycardia

Adverse Reactions

- Nausea
- Diarrhea
- Fatigue
- Cough
- Headache
- ILD/pneumonitis
- Hypertension
- Bradycardia
- Visual disturbances
- CPK elevation
- Pancreatic enzyme elevation
- Hyperglycemia
- Possible infertility in males

Mechanism of Action

- Brigatinib is a tyrosine kinase inhibitor with in vitro activity against multiple kinases including ALK, ROS1, insulin-like growth factor-1 receptor (IGF-IR), and FLT-3, as well as EGFR deletion and point mutations
- It inhibits autophosphorylation of ALK and ALK-mediated phosphorylation of downstream signaling proteins STAT3, AKT, ERK1/2, and S6
- It is also inhibits in vitro proliferation of cell lines expressing EML4-ALK and NPM-ALK fusion proteins

Clinical Studies

- Alunbrig was studied in a two-arm, open-label, multi-center trial (**ALTA**; n=222) in adults with locally advanced or metastatic ALK-positive NSCLC who had progressed on crizotinib

Clinical Studies

- The **major efficacy outcome measure** was confirmed overall response rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST v1.1) evaluated by an Independent Review Committee (IRC)
- Other efficacy outcomes were Investigator assessed ORR, duration of response (DOR), intracranial ORR, and intracranial DOR

Clinical Studies

- Patients were randomized to Alunbrig either 90mg once daily or 180mg once daily following a 7-day lead-in at 90mg once daily (90→180mg)
- Randomization was stratified by presence of brain metastases and best prior response to crizotinib
- Median duration of follow up was 8 months

Clinical Studies

- The IRC evaluated ORR was **48%** with 90mg once daily **53%** with 90→180mg once daily
- The IRC evaluated median duration of response (DOR) was **13.8 months** for both 90mg once daily and 90→180mg once daily

Clinical Studies

- The Investigator assessed ORR was **45%** with 90mg once daily and **54%** with 90→180mg once daily
- The Investigator assessed median duration of response was **13.8 months** with 90mg once daily and **11.1 months** with 90→180mg once daily

Clinical Studies

- IRC assessment of **intracranial ORR** and **intracranial DOR** was assessed in a subgroup of patients with brain metastases **(n=44)**
- Duration of intracranial response was measured from the date of first intracranial response until intracranial disease progression or death

Clinical Studies

- Intracranial ORR was **42%** and **67%** for 90mg once daily and 90→180mg once daily, respectively.
- Of the 23 patients that exhibited an intracranial response 78% of patients in the 90mg arm and 68% of the patients in the 90→180mg arm maintained a **response for ≥4 months**
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

http://www.empr.com/alunbrig/drug/34674/