ALK (Brigatinib) Innerleaf design Revise

Color: Pantone Metallic Coated 8483 C L - 195 mm X W - 255 mm

ALK™
Brigatinib

Jenphar Bangladesh | جـنـفـار بنغلاديش

Composition:
ALK 90 Tablet: Each film coated tablet contains Brigatinib INN 90 mg.

Pharmacology:
Brigatinib is a tyrosine kinase inhibitor 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 inhibits auto phosphorylation of ALK and ALK-mediated phosphorylation of the downstream signaling proteins STAT3, AKT, ERK1/2 and S6. Brigatinib also inhibits the proliferation of cell lines expressing EML4-ALK and NPM-ALK fusion proteins.
Brigatinib inhibits the viability of cells expressing EML4-ALK and 17 mutant forms associated with resistance to ALK inhibitors including Crizotinib, as well as EGFR-Del (E746-A750), ROS1-L2026M, FLT3-F691L and FLT3-D835Y. Brigatinib exhibits antitumor activity against 4 mutant forms of EML4-ALK, including G1202R and L1196M mutants identified in NSCLC tumors in patients who have progressed on Crizotinib.

Indication:
Brigatinib is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC).

Dose & administration:
90 mg orally once daily for the first 7 days; if tolerated, increase to 180 mg orally once daily. May be taken with or without food.

Table: Recommended Dosage Reductions of Brigatinib for Adverse Reactions

Dosage	First Dosage Reduction To	Second Dosage Reduction To	Third Dosage Reduction To
90 mg once daily	60 mg once daily	Permanently discontinue	N/A
180 mg once daily	120 mg once daily	90 mg once daily	60 mg once daily

Contra-indication:
None.

Warning and precaution:
Interstitial Lung Disease (ILD)/Pneumonitis:
Monitor for new or worsening respiratory symptoms, particularly during the first week of treatment. Withhold Brigatinib for new or worsening respiratory symptoms and promptly evaluate for ILD/pneumonitis. Upon recovery, either dose reduce or permanently discontinue Brigatinib.

Hypertension: Monitor blood pressure after 2 weeks and then at least monthly during treatment. For severe hypertension, withhold Brigatinib, then dose reduce or permanently discontinue.

Bradycardia: Monitor heart rate and blood pressure regularly during treatment. If symptomatic, withhold Brigatinib, then dose reduce or permanently discontinue.

Visual Disturbance: Advise patients to report visual symptoms. Withhold Brigatinib and obtain ophthalmologic evaluation, then dose reduce or permanently discontinue Brigatinib.

Creatine Phosphokinase (CPK) Elevation: Monitor CPK levels regularly during treatment. Based on the severity and with muscle pain or weakness, withhold Brigatinib, then resume or reduce dose.

Pancreatic Enzymes Elevation: Monitor lipase and amylase levels regularly during treatment. Based on the severity, withhold Brigatinib, then resume or reduce dose.

Hyperglycemia: Assess fasting serum glucose prior to starting Brigatinib and regularly during treatment. If not adequately controlled with optimal medical management, withhold Brigatinib, then consider dose reduction or permanently discontinue, based on severity.

Photosensitivity: Advise patients to limit sun exposure. Based on severity withhold Brigatinib, then resume at the same dose, reduce the dose, or permanently discontinue.

Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.

Side Effects:
The most common adverse reactions (≥25%) with Brigatinib are diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting, dyspnea, Liver enzyme elevation, Hyperglycemia, Creatine phosphokinase (CPK) elevation & Pancreatic enzymes elevation.
The most common serious adverse reactions are ILD/pneumonitis, pyrexia, dyspnea, pulmonary embolism, and asthenia.

Use in Specific Populations:
Pregnancy: Brigatinib is not recommended during pregnancy unless the benefit outweighs the risk to the baby.
Breast-feeding: Do not breast-feed during treatment with Brigatinib. It is unknown if Brigatinib passes into breast milk and could potentially harm the baby.
Pediatric Use: The safety and effectiveness of Brigatinib in pediatric patients have not been established.
Geriatric Use: No overall differences in safety or effectiveness were observed between patients ≥65 years and younger patients.
Hepatic Impairment: No dose adjustment is recommended for patients with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B). Reduce the dose of Brigatinib for patients with severe hepatic impairment.
Renal Impairment: No dose adjustment is recommended for patients with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B).Reduce the dose of Brigatinib for patients with severe renal impairment.

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

Overdose:
There is no specific antidote for overdose with Brigatinib. In the event of an overdose, monitor the patient for adverse reactions and provide appropriate supportive care.

Storage:
Store in a cool and dry place below 30^{0}C, protect from light. Keep out of the reach of children.

Packing:
ALK 90 Tablet: Each box contains 7 film coated tablets and one packet silica gel in a sealed container.

Manufactured by:
Jenphar Bangladesh Ltd.
Sreepur, Gazipur, Bangladesh

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