Alkenib (Lapatinib INN) Innerleaf design (English)

Pantone Metallic Coated 8483 C **W- 195 mm X H - 307 mm**

Alkenib™
Lapatinib

Jenphar Bangladesh | جـنـفـار بنغلاديش

Composition:
Alkenib Tablet: Each film-coated tablet contains Lapatinib INN 250 mg.

Pharmacology:
Lapatinib is a 4-anilinoquinazoline kinase inhibitor of the intracellular tyrosine kinase domains of both Epidermal Growth Factor Receptor (EGFR [ErbB1]) and of Human Epidermal Receptor Type 2 (HER2 [ErbB2]) receptors (estimated Kiapp values of 3nM and 13nM, respectively) with a dissociation half-life of greater than or equal to 300 minutes. Lapatinib inhibits ErbB-driven tumor cell growth in vitro and in various animal models.

Indication:
Lapatinib, a kinase inhibitor, is indicated in combination with:
(1) Capecitabine, for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
(2) Letrozole for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated. Lapatinib in combination with an aromatase inhibitor has not been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

Dose & administration:
HER2-Positive metastatic Breast Cancer: The recommended dose of Lapatinib is 1,250 mg given orally once daily on Days 1-21 continuously in combination with Capecitabine 2,000 mg/m2/day (administered orally in 2 doses approximately 12 hours apart) on Days 1-14 in a repeating 21-day cycle. Lapatinib should be taken at least one hour before or one hour after a meal. The dose of Lapatinib should be once daily (5 tablets administered all at once); dividing the daily dose is not recommended. Capecitabine should be taken with food or within 30 minutes after food. If a day's dose is missed, the patient should not double the dose the next day. Treatment should be continued until disease progression or unacceptable toxicity occurs.

Hormone Receptor-Positive, HER2-Positive Metastatic Breast Cancer: The recommended dose of Lapatinib is 1,500 mg given orally once daily continuously in combination with Letrozole. When coadministered with Lapatinib, the recommended dose of Letrozole is 2.5 mg once daily. Lapatinib should be taken at least one hour before or one hour after a meal. The dose of Lapatinib should be once daily (6 tablets administered all at once); dividing the daily dose is not recommended.

Dose modifications:
Cardiac events: Lapatinib should be discontinued in patients with a decreased left ventricular ejection fraction (LVEF). Lapatinib in combination with Capecitabine may be restarted at a reduced dose (1,000 mg/day) and in combination with Letrozole may be restarted at a reduced dose of 1,250 mg/day after a minimum of 2 weeks if the LVEF recovers to normal and the patient is asymptomatic.

Hepatic impairment: Patients with severe hepatic impairment (Child-Pugh Class C) should have their dose of Lapatinib reduced. A dose reduction from 1,250 mg/day to 750 mg/day (HER2-positive metastatic breast cancer indication) or from 1,500 mg/day to 1,000 mg/day (hormone receptor-positive, HER2-positive breast cancer indication) in patients with severe hepatic impairment is predicted to adjust the area under the curve (AUC) to the normal range and should be considered. However, there are no clinical data with this dose adjustment in patients with severe hepatic impairment.

Diarrhea: Lapatinib should be interrupted in patients with diarrhea which is NCI CTCAE Grade 3 or Grade 1 or 2 with complicating features (moderate to severe abdominal cramping, nausea or vomiting greater than or equal to NCI CTCAE Grade 2, decreased performance status, fever, sepsis, neutropenia, frank bleeding, or dehydration). Lapatinib may be reintroduced at a lower dose (reduced from 1,250 mg/day to 1,000 mg/day or from 1,500 mg/day to 1,250 mg/day) when diarrhea resolves to Grade 1 or less. Lapatinib should be permanently discontinued in patients with diarrhea which is NCI CTCAE Grade 4.

Concomitant strong CYP3A4 inhibitors: The concomitant use of strong CYP3A4 inhibitors should be avoided (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole). Grapefruit may also increase plasma concentrations of Lapatinib and should be avoided. If patients must be coadministered, a strong CYP3A4 inhibitor, based on pharmacokinetic studies, a dose reduction to 500 mg/day of Lapatinib is predicted to adjust the Lapatinib AUC to the range observed without inhibitors and should be considered. However, there are no clinical data with this dose adjustment in patients receiving strong CYP3A4 inhibitors.

Concomitant strong CYP3A4 inducers: The concomitant use of strong CYP3A4 inducers should be avoided (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital, St. John's wort). If patients must be coadministered a strong CYP3A4 inducer, based on pharmacokinetic studies, the dose of Lapatinib should be titrated gradually from 1,250 mg/day up to 4,500 mg/day (HER2-positive metastatic breast cancer indication) or from 1,500 mg/day up to 5,500 mg/day (hormone receptor-positive, HER2-positive breast cancer indication) based on tolerability. However, there are no clinical data with this dose adjustment in patients receiving strong CYP3A4 inducers. If the strong inducer is discontinued the Lapatinib dose should be reduced to the indicated dose.

Other toxicities: Discontinuation or interruption of dosing with Lapatinib may be considered when patients develop greater than or equal to Grade 2 NCI CTCAE toxicity, and can be restarted at the standard dose of 1,250 or 1,500 mg/day when the toxicity improves to Grade 1 or less. If the toxicity recurs, then Lapatinib in combination with Capecitabine should be restarted at a lower dose (1,000 mg/day) and in combination with Letrozole should be restarted at a lower dose of 1,250 mg/day.

Contra-indication:
Lapatinib is contraindicated in patients with known severe hypersensitivity (e.g., anaphylaxis) to this product or any of its components.

Warning & precaution:
1. Decreases in left ventricular ejection fraction have been reported. Confirm normal LVEF before starting Lapatinib and continue evaluations during treatment.
2. Lapatinib has been associated with hepatotoxicity. Monitor liver function tests before initiation of treatment, every 4 to 6 weeks during treatment, and as clinically indicated. Discontinue and do not restart Lapatinib if patients experience severe changes in liver function tests.
3. Dose reduction in patients with severe hepatic impairment should be considered.
4. Diarrhea, including severe diarrhea, has been reported during treatment. Manage with anti-diarrheal agents, and replace fluids and electrolytes if severe.
5. Lapatinib has been associated with interstitial lung disease and pneumonitis. Discontinue Lapatinib if patients experience severe pulmonary symptoms.
6. Lapatinib may prolong the QT interval in some patients. Consider ECG and electrolyte monitoring.
7. Severe cutaneous reaction have been reported. Discontinue Lapatinib if life threatening reactions are suspected.
8. Fetal harm can occur when administered to a pregnant woman. Women should be advised not to become pregnant when taking Lapatinib.

Adverse effects:
The most common (>20%) adverse reactions during treatment with Lapatinib plus capecitabine were diarrhea, palmar-plantar erythrodysesthesia, nausea, rash, vomiting, and fatigue. The most common (≥20%) adverse reactions during treatment with Lapatinib plus letrozole were diarrhea, rash, nausea, and fatigue.

Use in specific populations:
Pregnancy: Lapatinib can cause fetal harm when administered to a pregnant woman.

Lactation: There are no data on the presence of Lapatinib in human milk, or its effects on the breastfed child, or milk production.

Females and males of reproductive potential:
Females: Based on findings in animal studies, Lapatinib can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with Lapatinib and for 1 week after the last dose.

Males: Based on findings in animal reproduction studies, advise male patients with female partners of reproductive potential to use effective contraception during treatment with Lapatinib and for 1 week after the last dose.

Pediatric use: The safety and effectiveness of Lapatinib in pediatric patients have not been established.

Geriatric use: No overall differences in safety or effectiveness were observed between elderly subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Renal impairment: Lapatinib have not been specifically studied in patients with renal impairment or in patients undergoing hemodialysis. There is no experience with Lapatinib in patients with severe renal impairment.

Hepatic impairment: Systemic exposure (AUC) to lapatinib after a single oral 100-mg dose increased approximately 14% and 63% in subjects with moderate and severe preexisting hepatic impairment, respectively. Administration of Lapatinib in patients with severe hepatic impairment should be undertaken with caution due to increased exposure to the drug.

Drug interaction:
1. Lapatinib is likely to increase exposure to concomitantly administered drugs which are substrates of CYP3A4, CYP2C8, or P-glycoprotein (ABCB1).
2. Avoid strong CYP3A4 inhibitors. If unavoidable, consider dose reduction of Lapatinib in patients coadministered a strong CYP3A4 inhibitor.
3. Avoid strong CYP3A4 inducers. If unavoidable, consider gradual dose increase of Lapatinib in patients coadministered a strong CYP3A4 inducer.

Overdose:
There is no known antidote for overdoses of Lapatinib. The maximum oral doses of Lapatinib that have been administered in clinical trials are 1,800 mg once daily. More frequent ingestion of Lapatinib could result in serum concentrations exceeding those observed in clinical trials and could result in increased toxicity. Therefore, missed doses should not be replaced and dosing should resume with the next scheduled daily dose. Lapatinib is not significantly renally excreted and is highly bound to plasma proteins, hemodialysis would not be expected to be an effective method to enhance the elimination of Lapatinib. Treatment of overdose with Lapatinib should consist of general supportive measures.

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

Packing:
Alkenib Tablet: Each box contains 30 film coated tablets and one packet silica gel in a sealed HDPE container.

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

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