Certus

Lapatinib Ditosylate

COMPOSITION

Certus Tablet : Each film coated tablet contains Lapatinib Ditosylate INN equivalent to Lapatinib 250 mg.

Indication and Use :

Lapatinib is a kinase inhibitor indicated in combination with Capecitabine, for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a Taxane, and Trastuzumab. Lapatinib is also indicated in combination with 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.

MECHANISM OF ACTION

Lapatinib Works Inside Cells to Block the HER2 Pathway:

Lapatinib is a small molecule that passes through the cell membrane and binds to the part of HER2 found inside the cell. HER2 inhibition is believed to play a role in interrupting the signaling cascade associated with cell proliferation and tumor growth. Lapatinib inhibits 2 receptors involved in tumor proliferation-HER2 and its coreceptor, EGFR- resulting in an inhibition of ErbB-driven cell growth as seen in vitro and in various animal models.

DOSAGE AND ADMINISTRATION

Recommended Dosing 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.

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 Modification Guidelines

Cardiac Events : Lapatinib should be discontinued in patients with a decreased left ventricular ejection fraction (LVEF) that is Grade 2 or greater by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) and in patients with an LVEF that drops below the institution's lower limit of normal. 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 40 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.

DRUG-DRUG INTERACTIONS

Concomitant Strong CYP3A4 Inhibitors : The concomitant use of strong CYP3A4 inhibitors is (e.g., Ketoconazole, Itraconazole, Clarithromycin, Indinavir, Nefazodone, Ritonavir, Voriconazole) should be avoided. Grapefruit may also increase plasma concentrations of Lapatinib and should be avoided.

Concomitant Strong CYP3A4 Inducers : The concomitant use of strong CYP3A4 inducers (e.g., Dexamethasone, Phenytoin, Carbamazepine, Rifampin, Rifabutin, 61 Rifapentin, Phenobarbital) also should be avoided.

CONTRAINDICATIONS

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

ADVERSE REACTIONS

HER2 Positive Metastatic Breast Cancer: In clinical trial the most common adverse reactions (>20%) during therapy with Lapatinib plus Capecitabine were gastrointestinal (diarrhea, nausea, and vomiting) dermatologic (palmar149 plantar erythrodysesthesia and rash), and fatigue. Diarrhea was the most common adverse resulting in discontinuation of study medication. The most common Grade 3 and 4 adverse reactions (NCI CTCAE v3) were diarrhea and palmar-plantar erythrodysesthesia.

Hormone Receptor Positive, Metastatic Breast Cancer :

In clinical trial, Lapatinib has found to be associated with hepatotoxicity,interstitial lung disease /pneumotitisetc in some cases.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category D : Based on findings in animals, Lapatinib can cause fetal harm when administered to a pregnant woman.

Nursing Mothers : It is not known whether Lapatinib is excreted in human milk. Lapatinib should be used in nurses with caution benefits outweights the risk potential.

Pediatric Use : No overall differences in safety or effectiveness in between elderly subjects and younger subjects

Renal Impairment : There is no experience with Lapatinib in patients with severe renal impairment. However, renal impairment is unlikely to affect the pharmacokinetics of lapatinib given that less than 2% (lapatinib and metabolites) of an administered dose is eliminated by the kidneys.

Hepatic Impairment : Administration of Lapatinib in patients with severe hepatic impairment should be undertaken with caution due to increased exposure to the drug. A dose reduction should be considered for patients with severe pre-existing hepatic impairment. In patients who develop severe hepatotoxicity while on therapy, Lapatinib. should be discontinued and patients should not be retreated with Lapatinib.

Storage Condition : Keep out of the reach of children. Store below 30°C, dry place and away from light.

Presentration and packaging :

Each commercial box contains 35 Tablets in a HDPE pot.

Manufactured by-
BEACON®
Pharmaceuticals Limited
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