NIBALAP

Lapatinib INN 250 mg

COMPOSITION

NIBALAP 250 mg Tablet: Each film coated tablet contains Lapatinib Ditosylate Monohydrate INN 405 mg equivalent to Lapatinib 250 mg.

CLINICAL PHARMACOLOGY

Mechanism of action: Lapatinib, a 4-anilinoquinazoline, is an inhibitor of the intracellular tyrosine kinase domains of both EGFR (ErbB1) and of HER2 (ErbB2) receptors with a slow off-rate from these receptors (half-life greater than or equal to 300 minutes). Lapatinib inhibits ErbB-driven tumour cell growth. The combination of Lapatinib and Trastuzumab may offer complementary mechanisms of action as well as possible non-overlapping mechanisms of resistance.

Pharmacokinetics: ***Absorption:*** Absorption following oral administration of Lapatinib is incomplete and variable. Serum concentrations appear after a median lag time of 0.25 hours and peak plasma concentrations (Cmax) are achieved approximately 4 hours after administration. Daily dosing of Lapatinib results in achievement of steady state within 6 to7 days, indicating an effective half-life of 24 hours. ***Distribution:*** Lapatinib is highly bound (>99%) to albumin and alpha-1 acid glycoprotein. ***Metabolism:*** Lapatinib undergoes extensive metabolism, primarily by CYP3A4 and CYP3A5, with minor contributions from CYP2C19 and CYP2C8 to a variety of oxidated metabolites. ***Elimination:*** At clinical doses, the terminal phase half-life following a single dose was 14.2 hours; accumulation with repeated dosing indicates an effective half-life of 24 hours. Elimination of Lapatinib is predominantly through metabolism by CYP3A4/5 with negligible (<2%) renal excretion. Recovery of parent Lapatinib in feces accounts for a median of 27% (range 3 to 67%) of an oral dose.

INDICATIONS

NIBALAP is indicated in combination with:

- 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.
- 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.

DOSAGE AND ADMINISTRATION

- The recommended dosage of NIBALAP for advanced or metastatic breast cancer is 1,250 mg (5 tablets) given orally once daily on Days 1-21 continuously in combination with Capecitabine 2,000 mg/m^2/day (administered orally in 2 divided doses approximately 12 hours apart) on Days 1-14 followed by a 7 days rest period in a repeating 21 day cycle.
- The recommended dose of NIBALAP for hormone receptor positive, HER2 positive metastatic breast cancer is 1500 mg (6 tablets) given orally once daily continuously in combination with Letrozole 2.5 mg once daily.

NIBALAP should be taken once daily, do not divide the daily doses. NIBALAP should be taken at least one hour before or one hour after a meal. However, Capecitabine should be taken with food or within 30 minutes after a meal.

CONTRAINDICATIONS

Lapatinib is contraindicated in patients with known severe hypersensitivity (e.g., anaphylaxis) to this product.

ADVERSE REACTIONS

Common (>20%) adverse reactions during treatment with Lapatinib plus Capecitabine are diarrhea, palmar-plantar erythrodysesthesia, nausea, rash, vomiting, and fatigue. The most common (≥20%) adverse reactions during treatment with Lapatinib plus Letrozole are diarrhea, rash, nausea and fatigue.

PRECAUTIONS

Pregnancy: Pregnancy category D. Lapatinib can cause fetal harm when administered to a pregnant woman. Women should be advised not to become pregnant when taking Lapatinib. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. **Nursing mothers:** It is not known whether Lapatinib is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Lapatinib, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric use:** The safety and effectiveness of Lapatinib in pediatric patients have not been established. **Geriatric use:** No overall differences in safety or effectiveness has been observed between elderly subjects and younger subjects, but greater sensitivity of some older individuals cannot be ruled out. **Cardiovascular:** Confirm normal left ventricular ejection fraction before starting Lapatinib and continue evaluations during treatment. **Hepatic:** Monitor liver function tests before initiation of treatment, every 4 to 6 weeks during treatment. Discontinue and do not restart Lapatinib if patients experience severe changes in liver function tests. Dose reduction in patients with severe hepatic impairment should be considered. **Diarrhea:** Can be severe. Manage with anti-diarrheal agents, and replace fluids and electrolytes if severe. **Pulmonary:** Lapatinib has been associated with interstitial lung disease and pneumonitis. Discontinue Lapatinib if patients experience severe pulmonary symptoms.

DRUG INTERACTIONS

Lapatinib is likely to increase exposure to concomitantly administered drugs which are metabolized by CYP3A4 or CYP2C8 (Lapatinib can increase 24-hour systemic exposure (AUC) of Paclitaxel by 23%). Avoid strong CYP3A4 inhibitors; if unavoidable, consider dose reduction of Lapatinib in patients co-administered a strong CYP3A4 inhibitor (Ketoconazole, a CYP3A4 inhibitor, at 200 mg twice daily dose for 7 days increased AUC of Lapatinib by 3.6-fold and half-life by 1.7-fold of control). Avoid strong CYP3A4 inducers; if unavoidable, consider gradual dose increase of Lapatinib in patients co-administered a strong CYP3A4 inducer (Carbamazepine, at 100 mg twice daily dose for 3 days and 200 mg twice daily dose for 17 days, decreased AUC of Lapatinib by 72%).

OVERDOSE

There is no known antidote for overdoses of Lapatinib. The maximum oral doses of Lapatinib have been administered in clinical trials are 1,800 mg once daily, more frequent ingestion may result in serum concentrations exceeding those observed in clinical trials and may result in increased toxicity. Therefore, missed doses should not be replaced and dosing should resume with the next scheduled daily dose. Because 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.

STORAGE

Store below 30°C. Keep in a dry place away from light.

PRESENTATION

NIBALAP 250 mg Tablet: Each box contains 12 NIBALAP tablets in Alu-Alu blister pack.

Manufactured by:
ARISTOPHARMA LTD.
Shampur-Kadamtali I/A, Dhaka-Bangladesh

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