Erlotinib INN

ERTINIB

Tablet

Composition:

Ertinib 100 Tablet: Each film coated tablet contains Erlotinib Hydrochloride INN 109.28 mg equivalent to Erlotinib 100 mg.

Ertinib 150 Tablet: Each film coated tablet contains Erlotinib Hydrochloride INN 163.92 mg equivalent to Erlotinib 150 mg.

Clinical pharmacology:

Epidermal growth factor receptor (EGFR) is expressed on the cell surface of both normal and cancer cells. In some tumor cells signaling through this receptor plays a role in tumor cell survival and proliferation. Erlotinib is a tyrosine kinase inhibitor which reversibly inhibits the kinase activity of EGFR. It prevents autophosphorylation of tyrosine residues associated with the receptor and thereby inhibiting further downstream signaling. The absorption of this drug is 60%. Metabolism occurs in liver (CYP mediated, mainly CYP3A4 and a lesser extent by CYP1A2). This drug is eliminated by feces (83%) and urine (8%). It has a half-life ($t_{1/2}$) of 36.2 hours.

Indications:

Non-small cell lung cancer (NSCLC):

- Ertinib is indicated for the first-line treatment of patients with metastatic NSCLC.
- Ertinib is indicated for the maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
- It is also indicated for the treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.
- Ertinib is not recommended for use in combination with platinum-based chemotherapy.

Pancreatic cancer:

Ertinib in combination with Gemcitabine is indicated for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

Dosage & Administration:

Non-small cell lung cancer (NSCLC):

Ertinib 150 mg once daily taken on an empty stomach.

Pancreatic Cancer:

Ertinib 100 mg once daily taken on an empty stomach in combination with Gemcitabine.

Ertinib should be taken at least one hour before or two hours after the ingestion of food.

Contraindications:

Ertinib is contraindicated in patients who have a history of hypersensitivity reaction to any of its components.

Side effects:

Common adverse reactions: In more than 20% cases rash, diarrhea, anorexia, fatigue, dyspnea, cough, nausea, and vomiting occurs. **Interstitial Lung Disease (ILD):** Cases of serious ILD, including fatal cases, can occur with Erlotinib treatment (1.1%). **Hematologic:** The Erlotinib plus Gemcitabine combination may cause microangiopathic hemolytic anemia with thrombocytopenia (1.4%). **Dermatology:** Bullous, blistering and exfoliative skin conditions, including cases suggestive of Stevens-Johnson syndrome/Toxic epidermal necrolysis, which in some cases were fatal, can occur (0.4-1.2%). **Cardiac:** Erlotinib/gemcitabine combination may cause myocardial infarction (2.1%) and/or cerebrovascular accident (2.5%). **Ocular disorders:** Decreased tear production, abnormal eyelash growth, keratoconjunctivitis sicca or keratitis can occur (12.8-17.8%). **Renal failure:** Hepatorenal syndrome, severe acute renal failure including fatal cases, and renal insufficiency can occur with both the Erlotinib treatment (0.4%) and Erlotinib/Gemcitabine treatment (1.4%).

Precautions:

Pregnancy: Pregnancy category D. Erlotinib can cause fetal harm. Women should be advised to avoid becoming pregnant while receiving treatment with Erlotinib.

Nursing mothers: It is not known whether Erlotinib is excreted into human milk or not. 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 efficacy of Erlotinib has not been established in pediatric cases. **Geriatric Use:** The safety and efficacy of Erlotinib was similar in older and younger patients. **Hepatic Impairment:** Hepatotoxicity occurs with or without hepatic impairment, including hepatic failure and hepatorenal syndrome; monitor periodic liver testing. Erlotinib should be withheld or discontinued for severe or worsening liver tests.

Renal Impairment: Monitor renal function and electrolytes, particularly in patients at risk of dehydration. Withhold Erlotinib for severe renal toxicity.

Gastric: Patients receiving concomitant anti-angiogenic agents, corticosteroids, NSAIDs, or taxane-based chemotherapy, or who have prior history of peptic ulceration or diverticular disease may be at increased risk of gastrointestinal perforation (0.2-0.4%).

Patients taking anticoagulants: Severe and fatal hemorrhage can occur when Erlotinib and warfarin are administered concurrently. Regularly monitor prothrombin time and INR during Erlotinib treatment in patients taking warfarin or other coumarin-derivative anticoagulants.

Drug interactions:

CYP3A4 inducers: CYP3A4 inducers (rifampin, rifabutin, rifapentine, phenytoin, carbamazepine, phenobarbital, or St. John's Wort) reduces the AUC of Erlotinib. Avoid concomitant use, if possible. Increase Erlotinib doses by 50 mg increments at 2 week intervals to a maximum of 450 mg.

CYP3A4 inhibitors: CYP3A4 inhibitors (itraconazole, ketoconazole, voriconazole, atazanavir, indinavir, nelfinavir, ritonavir, saquinavir, clarithromycin, telithromycin, troleandomycin (TAO), nefazodone, or grapefruit or grapefruit juice) or with an inhibitor of both CYP3A4 and CYP1A2 (ciprofloxacin) increases the AUC of Erlotinib. Avoid concomitant use if possible. Reduce Erlotinib use by 50 mg decrements.

Drugs affecting gastric pH: Co-administration of Erlotinib with omeprazole decreased erlotinib AUC by 46% and co-administration of Erlotinib with ranitidine 300 mg decreased Erlotinib AUC by 33%. Avoid concomitant use of Erlotinib with proton pump inhibitors if possible. Separation of doses may not eliminate the interaction. If treatment with an H_2-receptor antagonist such as ranitidine is required, Erlotinib must be taken 10 hours after the H_2-receptor antagonist dosing and at least 2 hours before the next dose of the H_2-receptor antagonist. Although the effect of antacids on erlotinib pharmacokinetics has not been evaluated, the antacid dose and the Erlotinib dose should be separated by several hours, if an antacid is necessary.

Overdose:

Single oral doses of Erlotinib up to 1,000 mg in healthy subjects and weekly doses up to 1,600 mg in cancer patients have been tolerated. In case of suspected overdose, Erlotinib should be withheld and symptomatic treatment instituted.

Storage & Handling:

Store below 30^{o}C, keep in dry place & protect from sun light.

Presentation:

Ertinib 100 Tablet: Each box contains 10 Erlotinib 100 mg tablets in Alu-Alu blister pack. **Ertinib 150 Tablet:** Each box contains 10 Erlotinib 150 mg tablets in Alu-Alu blister pack.

Manufactured by:
ARISTOPHARMA LTD.
SHAMPUR-DHAKA-BANGLADESH

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