Oncology Product

ERLOREN

Erlotinib 100mg & 150mg

COMPOSITION

ERLOREN 100 Tablet: Each film coated tablet contains Erlotinib Hydrochloride INN 109.27 mg equivalent to 100 mg Erlotinib base.

ERLOREN 150 Tablet: Each film coated tablet contains Erlotinib Hydrochloride INN 163.90 mg equivalent to 150 mg Erlotinib base.

CLINICAL PHARMACOLOGY

ERLOREN potently inhibits the intracellular phosphorylation of HER1/EGFR receptor. HER1/EGFR receptor is expressed on the cell surface of normal cells and cancer cells. In non-clinical models, inhibition of EGFR phosphotyrosine results in cell stasis and/or death.

Pharmacodynamics/Kinetics

Absorption

Oral **ERLOREN** is well absorbed and has an extended absorption phase, with mean peak plasma levels occurring at 4 hours after oral dosing. A study in normal healthy volunteers provided an estimate of bioavailability of 59%. The exposure after an oral dose may be increased by food.

Distribution

ERLOREN has a mean apparent volume of distribution of 232 L and distributes into tumour tissue of humans. In a study of 4 patients (3 with NSCLC and 1 with laryngeal cancer) receiving 150 mg daily oral doses of Erlotinib, tumour samples from surgical excisions on Day 9 of treatment revealed tumour concentrations of Erlotinib that averaged 1,185 ng/g of tissue. This corresponded to an overall average of 63% of the steady state observed peak plasma concentrations. The primary active metabolites were present in tumours at concentrations averaging 160 ng/g tissue, which corresponded to an overall average of 113% of the observed steady state peak plasma concentrations.

Metabolism

ERLOREN is metabolised in humans by hepatic cytochrome P450 enzymes, primarily by CYP3A4 and to a lesser extent by CYP1A2. Extrahepatic metabolism by CYP3A4 in intestine, CYP1A1 in lung and CYP1B1 in tumour tissue potentially contribute to the metabolic clearance of Erlotinib. In vitro studies indicate approximately 80 - 95% of Erlotinib metabolism is by the CYP3A4 enzyme. There are three main metabolic pathways identified: 1) O-demethylation of either side chain or both, followed by oxidation to the carboxylic acids; 2) oxidation of the acetylene moiety followed by hydrolysis to the aryl carboxylic acid; and 3) aromatic hydroxylation of the phenyl-acetylene moiety.

Elimination

The metabolites and trace amounts of Erlotinib are excreted predominantly via the faeces (>90%), with renal elimination accounting for only a small amount of an oral dose.

Clearance

Erlotinib showed a mean apparent clearance of 4.47 L/hour with a median half-life of 36.2 hours. Therefore, the time to reach steady state plasma concentration would be expected to occur in approximately 7 - 8 days. No significant relationships between predicted apparent clearance and patient age, body weight, gender and ethnicity were observed.

INDICATIONS

ERLOREN is indicated for-

- Frst-line treatment of non-small cell lung cancer
- Maintenance treatment of non-small cell lung cancer
- Pancreatic cancer

DOSAGE AND ADMINISTRATION

STANDARD DOSAGE

Non-small cell lung cancer (NSCLC)

The recommended daily dose of **ERLOREN** is 150 mg taken on an empty stomach at least one hour before or two hours after the ingestion of food.

Pancreatic Cancer

The recommended daily dose of **ERLOREN** is 100 mg taken on an empty stomach at least one hour before or two hours after the ingestion of food.

Special Dosage Instructions

Concomitant use of CYP 3A4 substrates and modulators may require dose adjustment. When dose adjustment is necessary, it is recommended to reduce in 50 mg increments.

Paediatric use: The safety and efficacy of Erlotinib has not been studied in patients under the age of 18 years.

Smokers: Cigarette smoking has been shown to reduce Erlotinib exposure by 50 - 60%.

Use in Special Populations

Pregnancy

Women of childbearing potential must be advised to avoid pregnancy while on **ERLOREN**. Adequate contraceptive methods should be used during therapy and for at least 2 weeks after completing therapy. Treatment should only be continued in pregnant women if the potential benefit to the mother outweighs the risk to the foetus.

Nursing mothers

It is not known whether Erlotinib is excreted in human milk. Because of the potential harm to the infant, mothers should be advised against breastfeeding while receiving **ERLOREN**.

Hepatic impairment

ERLOREN is eliminated by hepatic metabolism and biliary excretion. Erlotinib exposure was similar in patients with moderately impaired hepatic function (Child-Pugh score 7 - 9) compared with patients with adequate hepatic function, including patients with primary liver cancer or hepatic metastases. **ERLOREN** dosing should be interrupted or discontinued if changes in liver function are severe.

CONTRAINDICATIONS

ERLOREN is contraindicated in patients with severe hypersensitivity to Erlotinib or to any component of Erlotinib.

PRECAUTIONS

Interstitial lung disease

Cases of interstitial lung disease (ILD)-like events, including fatalities, have been reported uncommonly in patients receiving Erlotinib for treatment of NSCLC or other advanced solid tumours. **ERLOREN** should be discontinued and appropriate treatment initiated as necessary.

Diarrhoea, dehydration, electrolyte imbalance and renal failure

Diarrhoea has occurred in patients on Erlotinib and moderate or severe diarrhoea should be treated with loperamide. In some cases, dose reduction may be necessary.

Hepatitis, hepatic failure

ERLOREN dosing should be interrupted or discontinued if changes in liver function are severe such as a doubling of total bilirubin and/or a tripling of transaminases relative to pre-treatment levels.

Gastrointestinal perforation

Patients receiving concomitant anti-angiogenic agents, corticosteroids, NSAIDs and/or taxane based chemotherapy, or who have prior history of peptic ulceration or diverticular disease are at increased risk. **ERLOREN** should be permanently discontinued in patients who develop gastrointestinal perforation.

Bullous and exfoliative skin disorders

Bullous, blistering and exfoliative skin conditions have been reported; **ERLOREN** treatment should be interrupted or discontinued if the patient develops severe bullous, blistering or exfoliating conditions.

Ocular disorders

ERLOREN therapy should be interrupted or discontinued if patients present with acute/worsening ocular disorders such as eye pain.

ADVERSE EFFECTS

Nausea, vomiting, loss of appetite, mouth sores, dry skin, or eye irritation may occur. Changes in diet such as eating several small meals or limiting activity may help lessen the chance of nausea.

Diarrhea is a common side effect. Rare but very serious side effects occur: black stools, vomit that looks like coffee grounds, easy bleeding/bruising, stomach/abdominal pain, yellowing eyes or skin, dark urine, unusual fatigue, signs of infection (e.g., fever, chills, persistent sore throat), new or worsening shortness of breath or cough.

ERLOREN can commonly cause a mild rash that is usually not serious. However, you may not be able to tell it apart from a rare rash that could be a sign of a severe allergic reaction.

DRUG INTERACTIONS

ERLOREN is metabolized predominantly by CYP3A4, and inhibitors of CYP3A4 would be expected to increase exposure.

PHARMACEUTICAL INFORMATION

Storage condition

Store in a cool (below 30˚C) and dry place, away from light. Keep out of the reach of children.

Packaging

ERLOREN 100 Tablet: Each commercial box contains 1×7 tablets in Alu-PVC blister pack.

ERLOREN 150 Tablet: Each commercial box contains 1×7 tablets in Alu-PVC blister pack.

Marketed by
Renata Limited
Mirpur, Dhaka, Bangladesh.

Manufactured by
Renata Oncology
Rajendrapur, Gazipur, Bangladesh.
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