KIMOTAR® F.C. Tablet
Erlotinib

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Composition
Each F.C. Tablet KIMOTAR® 150 mg contains: Erlotinib (as Hydrochloride) 150 mg.

Description
Kimotar® inhibits the intracellular phosphorylation of tyrosine kinase associated with the epidermal growth factor receptor. Kimotar® expressed on the cell surface of healthy cells and cancer cells, and prevents autophosphorylation of tyrosine residues associated with the receptor, thereby inhibiting further downstream signaling. It is used for the management of locally advanced or metastatic non-small cell lung cancer either in disease that is unresponsive to other therapy, or as maintenance monotherapy in those with stable disease after platinum-based first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

Pharmacokinetic
Absorption
60% absorbed and peak plasma levels occur 4 hours after a dose. Decrease in pH increase the solubility of Kimotar.

Distribution
Protein binding: Approximately 93%
Kimotar Bioavailability is increased by Food to almost 100%.
Metabolism
Liver By CYP3A4 AND CYP1A2.
Elimination
Half-life elimination: 36.2 hours.
Excretion
83% in Faces and 8% in urine.

Dosage and Administration
Adult

1. None-Small cell lung cancer
For the first-line treatment of metastatic non-small cell lung cancer in which tumors have epidermal growth factor receptor (EGFR). maintenance treatment of locally advanced or metastatic non-small cell lung cancer when disease has not progressed after 4 cycles of platinum based first-line chemotherapy; treatment of locally advanced or metastatic non-small cell lung cancer after failure of at least 1 prior chemotherapy regimen:
150 mg daily.
Dosage reduction may be required for patients with hepatic impairment.

2. Pancreatic Cancer
First-line treatment of locally advanced, unresectable or metastatic pancreatic Cancer in Combination with gemcitabine:
100 mg Daily, in combination with gemcitabine.

3. Off-label uses
Treatment of squamous cell head and neck cancer:
150 mg orally once daily.
Higher doses cause increased toxicity without improved clinical benefit.

Dosage Adjustment
Discontinue therapy in patients whose abnormal liver tests do not improve significantly or resolve within 3 weeks. One guideline is shown in the following table. Monitor Patients with hepatic dysfunction closely, especially if total bilirubin is more than 3 times the upper limit of normal (ULN).
When restarting therapy following withholding treatment for a dose-limiting toxicity that has resolved to baseline or grade 1 or less, reduce the dose in 50 mg decrements.

Kimotar Adjustment Based on Hepatic Function

AST	Serum direct bilirubin	Recommendations
< 3 times the ULN	< 1mg/dL	No change to initial dosage
> 3 times the ULN	1 to 7 mg/dL	Reduce initial dosage to 75 mg/day. May gradually increase to labeled dosage as tolerated.
---	7 mg/dL	No information.

Monitor
- Perform periodic liver function tests; transaminases, bilirubin, and alkaline phosphatase; during treatment.
- Monitor patients with hepatic impairment.
- Regularly monitor patients taking Kimotar and warfarin or other coumarin-deviative anti-coagulants for changes in prothrombin time or international normalized ratio.
- Periodically monitor renal function and serum electrolytes in patients at risk of dehydration.
- Monitor patients for acute onset or progression of pulmonary symptoms.

Precautions/Warnings
• Interstitial lung disease:
In patients with interstitial lung disease, the onset of symptoms was 5 days to more than 9 months after initiating therapy. Withhold Kimotar for acute onset of new or progressive unexplained pulmonary symptoms such as dyspnea, cough, and fever pending diagnostic evaluation. If interstitial lung disease in confirmed, permanently discontinue therapy.

• Renal Effects:
Hepatorenal syndrome, Severe acute renal failure and renal insufficiency can occur with treatment. Withhold Kimotar in patients developing severe renal impairment until renal toxicity is resolved.

• Hepatotoxicity, Hepatic Function Impairment:
Hepatic failure can occur with Kimotar treatment in patient with normal hepatic function. Withhold Kimotar in patients without preexisting hepatic impairment for total bilirubin levels greater than 3 times the ULN or transaminases greater than 5 times the ULN. Discontinue Kimotar in patients whose abnormal liver tests do not improve significantly or resolve within 3 weeks.

• GI perforation:
Permanently discontinue treatment in patients who develop GI perforation.

• Dermatologic Effects:
Bullous, Blistering, and exfoliative skin conditions have been reported, including cases suggestive of Stevens-Johnson Syndrome, which in some cases were fatal.
Discontinue treatment if the patients develops severe dermatologic symptoms.

• Cardiovascular Effects:
Myocardial infraction/ischemia and cerebrovascular accident can increase in monotherapy lung cancer with Kimotar.

• Hematologic effects:
The incidence of microangiopathic hemolytic anemia with thrombocytopenia in monotherapy lung cancer with the Kimotar can occur.

• Ophthalmic effects:
Corneal perforation and ulceration can occur during treatment. Interrupt or discontinue Kimotar therapy if patients present with acute ocular disorders, such as eye pain.

Contraindication
Caution with concomitant use with hepatotoxic drugs-monitor liver function.

Adverse Effects
Abdominal pain, Anorexia, conjunctivitis, Depression, Diarrhea, Dry skin, dyspepsia, Fatigue, Flatulence, Headache, Neuropathy, Pruritus, Rigor, Eyelash changes, Gastro-intestinal perforation, Interstitial lung disease - discontinue if unexplained symptoms such as dyspnea, cough or fever occur, Hepatic failure, Corneal perforation, Corneal ulceration, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Alopecia, Bone-marrow suppression, Hyperuricemia, Nausea, Oral mucositis, thromboembolism, Tumor lysis syndrome and Vomiting.

Drug Interaction
Interact with Analgesics, Antacids, Antibacterials, Anticoagulants, Antifungals, Antipsychotics, Antivirals, Cytotoxics, Ulcer-healing Drugs.

Patient information
Advise patients to contact their health care provider if the following signs or symptoms occur. Inform patients that if they develop a skin rash, it commonly occurs on the face, upper chest, and back, and may occur or worsen in sun-exposed areas. Inform patients that skin reactions are anticipated when taking Kimotar; proactive intervention may include alcohol-free emollient cream and use of sunscreen or avoidance of sun exposure. Discuss the management of rash with the patient. This may include topical corticosteroids or antibiotics with anti-inflammatory properties. Acne preparations with drying properties may aggravate the dry skin and erythema. Treatment of rash has not been formally studied and should be based on rash severity. Inform patients that hyperpigmentation or dry skin, with or without digital skin fissures, may occur and that the majority of cases were associated with rash.
Inform patients that hair and nail disorders, including hirsutism and brittle and loose nails, may occur.
Inform Patients that diarrhea can usually be managed with loperamide.
Inform woman of reproductive potential to avoid becoming pregnant while taking Kimotar. Advise woman to use highly effective contraceptive methods during therapy and for at least 2 weeks after taking the last dose.
Advice pregnancy is suspected, during treatment.
Advise breast-feeding mothers to discontinue breast-feeding while receiving Kimotar.
Advice patients who smoke to stop smoking while taking Kimotar because cigarette smoking reduce plasma concentrations of Kimotar.

How to Use
Administer on an empty stomach at least 1 hour before or 2 hour after food. Administration with food increases bioavailability to almost 100%, which may cause increased toxicity. For patients unable to swallow tablets whole, place tablets in 100 ml of distilled water; do not crush tablet. Stir until dispersed, then have the patient drink the mixture immediately.

Pregnancy & Lactation
Pregnancy Category: D.
Lactation: it is not known whether Kimotar is excreted in human milk.

Storage
keep away from light and moisture, Store below 30°C. Do not store in the bathroom. Keep all medicine away from children and pets.

Presentation KIMOTAR®
Bottle of 30 F.C. Tablets

References
British National Formulary 2015,8th Section, Maligned Disease, Erlotinib , Page 807-808
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Martindale, Antineoplastic chapter, Erlotinib, Page 788-790

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