# KIMOTAR® (ERLOTINIB) F. C. TABLET

**KIMOTAR®**
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**KIMOTAR® (ERLOTINIB) F. C. TABLET FOR ORAL USE**
Read this patient information carefully before you start taking Kimotar® because it answers some common questions about Kimotar®. This medication is prescribed for your current condition, therefore do not use it in similar cases and do not recommend it to others.
To report SUSPECTED ADVERSE REACTIONS, contact Noavaran Daroui Kimia Co. at +982166433514 or send email to medical@kimia-pharma.co

**Read this patient information carefully before you start taking Kimotar® because it contains important information for you. This leaflet does not take the place of talking with your healthcare provider about your medical condition or treatment.**

## Composition
Each film-coated tablet Kimotar® 150 mg contains: Erlotinib (as HCl) 150 mg.

## Mechanism of action
Erlotinib reversibly inhibits overall epidermal growth factor receptor (HER1/EGFR) - tyrosine kinase activity.

## Pharmacokinetic
### Absorption
Kimotar® is about 60% absorbed and have peak plasma levels occuring 4 hours after oral administration. Food increased the bioavailability of Kimotar® to approximately 100%.
### Distribution
Kimotar® is 93% protein bound to plasma albumin and alpha-1 acid glycoprotein (AAG). Kimotar® has an apparent volume of distribution of 232 liters.
### Metabolism
Kimotar® is metabolized primarily by CYP3A4 and to a lesser extent by CYP1A2, and the extrahepatic isoform CYP1A1, *in vitro*.
### Excretion
Primarily as metabolites: Feces (83%; 1% as unchanged drug); urine (8%, 0.3% as unchanged drug)
### Elimination
Kimotar® is eliminated with a median half-life of 36.2 hours in patients receiving the single-agent Kimotar® 2nd/3rd line regimen. Time to reach steady state plasma concentration would therefore be 7-8 days.

## Indication
Kimotar® is a kinase inhibitor indicated for:
- The treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.
- First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

**Limitations of Use:**
- Safety and efficacy of Kimotar® have not been established in patients with NSCLC whose tumors have other EGFR mutations.
- Kimotar® is not recommended for use in combination with platinum-based chemotherapy.

## Dosage and Administration
- NSCLC: 150 mg orally, on an empty stomach, once daily.
- Pancreatic cancer: 100 mg orally, on an empty stomach, once daily.

## Side effects / Adverse reactions
**It should be noted that these side effects do not occur in all patients. These are not all the possible side effects of Kimotar®. For more information, ask your healthcare provider or pharmacist.**

**Kimotar® can cause serious side effects, including:**
- **Lung problems (called interstitial lung disease [ILD] events).** Kimotar® has been shown to cause lung problems that can be life-threatening. Symptoms of lung problems may include shortness of breath, cough, and fever. Kimotar® may need to be stopped if you have any of these symptoms.
- **Liver and kidney problems.** Kimotar® has been shown to cause severe kidney and liver problems that can be life-threatening. Some people had their kidneys and liver stop working. Let your healthcare provider know if you have a history of liver or kidney disease. Your healthcare provider should monitor your kidney function and electrolytes particularly if you are at risk of dehydration. Your healthcare provider will withhold Kimotar® for severe renal toxicity.
- **Stomach and intestinal problems (called gastrointestinal [GI] perforation).** Kimotar® has been shown to cause GI perforation problems that can be life-threatening. A GI perforation is a hole that develops in your stomach or intestine. Seek immediate medical attention if you have severe abdominal pain and discontinue Kimotar®. Kimotar® patients may be at a higher risk for GI perforation if they:
  - Are taking medicines including those that may help block the growth of blood vessels; steroids; non-steroidal anti-inflammatory drugs (NSAIDs); and certain chemotherapies. Always tell your healthcare provider about any medicines you are taking.
  - Have a history of ulcers or other stomach disease.
- **Skin rash, bullous and exfoliative skin disorders:** Kimotar® has been shown to cause blistering and skin peeling. skin reactions can occur or worsen on sun-exposed areas while taking Kimotar®. Hyperpigmentation or dry skin, with or without digital skin fissures, have been reported and in the majority of cases were associated with rash. Kimotar® can increase the risk of bullous and exfoliative skin disorders. Seek immediately medical attention for severe skin reactions and discontinue Kimotar®.
  - Hair and nails: Hair and nail problems have been seen in patients taking Kimotar®. These include increased hairiness and brittle or loose nails.
  - Your skin and nails may get darker. You may also have dry skin that may or may not crack. This most often happens with rash.
- **Blood, bleeding, and clotting problems.** Kimotar® has been shown to cause certain blood problems and other bleeding and clotting problems. These have led to stroke **(Cerebrovascular accident, CVA)** and can be life-threatening. The risk of CVA including cerebral hemorrhage is increased in patients with pancreatic cancer.
- **Microangiopathic hemolytic anemia (MAHA) with Thrombocytopenia:** The risk of MAHA is increased in patients with pancreatic cancer.
- **Eye disorders:** Kimotar® has been shown to cause dry eyes, unusual eyelash growth, or swelling of the cornea. The cornea is the clear coating of the eyeball. This swelling may irritate or damage the eye. If you develop eye signs or symptoms, lacrimation, light sensitivity, blurred vision, eye pain, red eye, or changes in vision, contact your healthcare provider. Discontinue Kimotar® for corneal perforation, ulceration or persistent severe keratitis.

**Call your healthcare provider right away if you have aforementioned symptoms.**

**The most common side effects of Kimotar® include:**
Rash, diarrhea, loss of appetite, tiredness, shortness of breath, cough, nausea, and vomiting.

## Drug interaction
- **CYP3A4 Inhibitors**
  Co-administration of Kimotar® with a strong CYP3A4 inhibitor or a combined CYP3A4 and CYP1A2 inhibitor increased Kimotar® exposure. Increased Kimotar® exposure may increase the risk of exposure-related toxicity. Kimotar® is metabolized primarily by CYP3A4 and to a lesser extent by CYP1A2.

  Avoid co-administering Kimotar® with strong CYP3A4 inhibitors (e.g., boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telithromycin, voriconazole, grapefruit or grapefruit juice) or a combined CYP3A4 and CYP1A2 inhibitor (e.g., ciprofloxacin). Reduce the Kimotar® dosage when co-administering with a strong CYP3A4 inhibitor or a combined CYP3A4 and CYP1A2 inhibitor if co-administration is unavoidable.
- **CYP3A4 Inducers**
  Pre-treatment with a CYP3A4 inducer prior to Kimotar® decreased Kimotar® exposure. Increase the Kimotar® dosage if co-administration with CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, rifabutin, rifapentine, phenobarbital and St. John's wort) is unavoidable.
- **CYP1A2 Inducers and Cigarette Smoking**
  Cigarette smoking decreased Kimotar® exposure. Avoid smoking tobacco (CYP1A2 inducer) and avoid concomitant use of Kimotar® with moderate CYP1A2 inducers (e.g., teriflunomide, rifampin, or phenytoin). Increase the Kimotar® dosage in patients that smoke tobacco or when co-administration with moderate CYP1A2 inducers is unavoidable.
- **Drugs that Increase Gastric pH**
  Co-administration of Kimotar® with proton pump inhibitors (e.g., omeprazole) and H-2 receptor antagonists (e.g., ranitidine, famotidine) decreased Kimotar® exposure. For proton pump inhibitors, avoid concomitant use if possible. For H-2 receptor antagonists and antacids, modify the dosing schedule. Increase the dose of Kimotar® when co-administered with gastric pH elevating agents is not likely to compensate for the loss of exposure.
  If the use of antacids is considered necessary during treatment with Kimotar®, they should be taken at least 4 hours before or 2 hours after the daily dose of Kimotar®.
- **Anticoagulants**
  Interaction with coumarin-derived anticoagulants, including warfarin, leading to increased International Normalized Ratio (INR) and bleeding adverse reactions, which in some cases were fatal, have been reported in patients receiving Kimotar®. Regularly monitor prothrombin time or INR in patients taking coumarin-derived anticoagulants. Dose modifications of Kimotar® are not recommended.
- **Erlotinib and P-glycoprotein inhibitors**
  Kimotar® is a substrate for the P-glycoprotein active substance transporter. Concomitant administration of inhibitors of Pgp, e.g. cyclosporine and verapamil, may lead to altered distribution and/or altered elimination of Kimotar®. The consequences of this interaction for e.g. CNS toxicity have not been established. Caution should be exercised in such situations.

## Warnings
**Before taking Kimotar®, tell your healthcare provider about all of your medical conditions including if you:**
- are taking other medicines that may increase or decrease the amount of Kimotar® in your blood or influence its effect (for example antifungals like ketoconazole, protease inhibitors (ritonavir), erythromycin, clarithromycin, phenytoin, carbamazepine, barbiturates, rifampicin, ciprofloxacin, omeprazole, ranitidine, famotidine, St. John's Wort or proteasome inhibitors (bortezomib)), talk to your doctor. In some cases these medicines may reduce the efficacy or increase the side effects of Kimotar® and your doctor may need to adjust your treatment. Your doctor might avoid treating you with these medicines while you are receiving Kimotar®.
- are taking anticoagulants (a medicine which helps to prevent thrombosis or blood clotting e.g. warfarin), Kimotar® may increase your tendency to bleed. Talk to your doctor, he will need to regularly monitor you with some blood tests.
- are taking statins (medicines to lower your blood cholesterol), Kimotar® may increase the risk of statin related muscle problems, which on rare occasions can lead to serious muscle breakdown (rhabdomyolysis) resulting in kidney damage, talk to your doctor. If you experience unexplained muscle pain, tenderness, weakness or cramps, your doctor may need to interrupt or stop your treatment.
- use contact lenses and/or have a history of eye problems such as severe dry eyes, inflammation of the front part of the eye (cornea) or ulcers involving the front part of the eye, tell your doctor.
- have sudden difficulty in breathing associated with cough or fever because your doctor may need to treat you with other medicines and interrupt your Kimotar® treatment.
- have diarrhea because your doctor may need to treat you with anti-diarrhea (for example loperamide).
- have severe or persistent diarrhea, nausea, loss of appetite, or vomiting immediately tell your doctor because your doctor may need to interrupt your Kimotar® treatment and may need to treat you in the hospital.
- have severe pain in the abdomen, severe blistering or peeling of skin. Your doctor may need to interrupt or stop your treatment.
- develop acute or worsening redness and pain in the eye, increased eye watering, blurred vision and/or sensitivity to light, please tell your doctor or nurse immediately as you may need urgent problems treatment.
- have ever had problems with your liver. Kimotar® may cause serious liver problems and some cases have been life-threatening. Your doctor may perform blood tests while you are taking this medicine to monitor whether your liver functions properly.

**Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.**

## Missed dose
If you miss one or more doses of Kimotar®, contact your doctor or pharmacist as soon as possible.
Do not take a double dose to make up for a forgotten dose.

## Overdose
Withhold Kimotar® in patients with an overdose or suspected overdose. Contact your doctor or pharmacist immediately.

## Pregnancy and lactation
Kimotar® may harm your unborn baby. Tell your healthcare provider right away if you are pregnant, or if you become pregnant during treatment with Kimotar®.
Use effective birth control (contraception) during treatment with Kimotar®, and for 1 month after the last dose.

Avoid breastfeeding during treatment with Kimotar® and for 2 weeks after the final dose.

## Patient information
- Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.
- The tablet should be taken at least one hour before or two hours after the ingestion of food.
- Skin reactions can occur or worsen on sun-exposed areas while taking Kimotar®. Use alcohol-free emollient cream and sunscreen or avoid sun exposure.
- If you get diarrhea during treatment, it can usually be managed with loperamide and contact your healthcare provider for severe or persistent diarrhea.
- It is better to stop smoking. Contact your health care provider for any changes in smoking status and that the dose of Kimotar® may need to be adjusted if they smoke.
- If you are taking warfarin or other coumarin-derivative anticoagulants, your healthcare provider should regularly monitor INR.
- DO NOT eat grapefruit or drink grapefruit juice before talking with your healthcare provider.
- Kimotar® contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking Kimotar®.

## Storage
- Keep away from light and moisture. Store below 30°C.
- Keep out of the reach of children.
- Keep in the original container.
- Keep the disciccant in the bottle. Do not eat or throw away desiccant pack.
- Safely throw away medicine that is out of date or that you no longer need. Ask your pharmacist how to safely throw away Kimotar® tablets.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

## Packaging
Bottle of 30 F. C. Tablets

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