GEFISA® (GEFITINIB) F. C. TABLET

GEFISA®
GEFITINIB

GEFISA® (GEFITINIB) TABLET FOR ORAL USE
Read this patient information carefully before you start taking Gefisa® because it answers some common questions about Gefisa®. 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 Gefisa® 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 Gefisa® 250 mg contains: Gefitinib 250 mg.

Mechanism of action
Gefitinib reversibly inhibits the kinase activity of wild-type and certain activating mutations of EGFR. Gefitinib binding affinity for EGFR exon 19 deletion or exon 21 point mutation L858R mutations is higher than its affinity for the wild-type EGFR.

Pharmacokinetic
Absorption
The mean oral bioavailability of Gefisa® is 60%, with peak plasma levels occurring 3-7 hours after dosing.
Distribution
Gefisa® is extensively distributed throughout the body with a mean steady state volume of distribution of 1400 L following intravenous administration.
Metabolism
Gefisa® undergoes extensive hepatic metabolism in humans, predominantly by CYP3A4.
Elimination
Gefisa® is cleared primarily by the liver, with total plasma clearance and elimination half-life of 48 hours after intravenous administration. Steady state plasma concentrations are achieved within 10 days after daily dosing.
Excretion
Excretion of Gefisa® and its metabolites is predominantly via the feces (86%), with renal elimination accounting for less than 4% of the administered dose.

Indication
Gefisa® is a tyrosine kinase inhibitor indicated for:

the first-line 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.

*Limitation of Use: Safety and efficacy of Gefisa® have not been established in patients whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

Dosage and administration
Recommended dose is 250 mg orally, once daily with or without food.

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 Gefisa®. For more information, ask your healthcare provider or pharmacist.
Gefisa® may cause serious side effects including:

- **lung or breathing problems.** Gefisa® may cause inflammation of the lung that may be life threatening. Symptoms may be similar to those symptoms from lung cancer. Tell your healthcare provider right away if you have any new or worsening lung problems, or any combination of the following symptoms: trouble breathing or shortness of breath, cough, or fever.
- **liver problems.** Gefisa® may cause inflammation of the liver that may be life threatening. Tell your healthcare provider right away if you have any symptoms of a liver problem which may include:
  - yellowing of your skin or the white part of your eyes (jaundice)
  - dark or brown (tea colored) urine
  - light-colored bowel movements (stools)
  - decreased appetite
  - pain on the right side of your stomach (abdomen)

Your healthcare provider will do blood tests to check your liver function during you treatment with Gefisa®.

- **a tear in the wall of your stomach or intestines (perforation).** Get emergency medical help right away if you have severe stomach (abdomen) pain.
- **diarrhea.** Diarrhea is common with Gefisa® and can sometimes be severe. Tell your healthcare provider right away if you have severe diarrhea or diarrhea that will not go away.
- **eye problems.** Tell your healthcare provider if you get watery eyes, sensitivity to light, blurred vision, eye pain, eye redness, or vision changes.
- **skin reactions.** Skin redness, rash, itching, and acne are common with Gefisa®. This may occur on any part of your body. Get medical help right away if you develop severe skin reactions such as peeling or blistering of your skin.

The most commonly reported adverse drug reactions (ADRs), reported in more than 20% of the patients and greater than placebo were :
skin reactions and diarrhea.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

Drug interaction
- Drugs that are strong inducers of CYP3A4 increase the metabolism of Gefisa® and decrease Gefisa® plasma concentrations. Increase Gefisa® to 500 mg daily in patients receiving a strong CYP3A4 inducer (e.g., rifampicin, carbamazepine, phenytoin, tricyclic antidepressant, barbiturates and St John's wort) and resume Gefisa® at 250 mg 7 days after discontinuation of the strong inducer.
- Drugs that are strong inhibitors of CYP3A4 (e.g., ketoconazole and itraconazole, posaconazole, voriconazole, protease inhibitors, clarithromycin, telithromycin) decrease Gefisa® metabolism and increase Gefisa® plasma concentrations. Monitor adverse reactions when administering strong CYP3A4 inhibitors with Gefisa®.
- Drugs that elevate gastric pH (e.g., proton pump inhibitors, histamine H2-receptor antagonists, and antacids) may reduce plasma concentrations of Gefisa®. Avoid concomitant use of Gefisa® with proton pump inhibitors, if possible. If treatment with a proton-pump inhibitor is required, take Gefisa® 12 hours after the last dose or 12 hours before the next dose of the proton-pump inhibitor. Take Gefisa® 6 hours after or 6 hours before an H2-receptor antagonist or an antacid.
- When the use of CYP2D6 substrates are considered in combination with Gefisa®, a dose modification of the CYP2D6 substrate should be considered especially for products with a narrow therapeutic window.

Warnings
Before taking Gefisa®, tell your healthcare provider about all of your medical conditions, including if you:
- have lung or breathing problems.
- ever had liver problems.
- have vision or eye problems.
- are pregnant or plan to become pregnant. Gefisa® can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Gefisa® passes into your breast milk. Do not breastfeed during treatment with Gefisa®.
- If you take a proton pump inhibitor (PPI), H2 blocker, or an antacid medicine, talk to your healthcare provider about the best time to take it during treatment with Gefisa®.
- If you take a blood thinner called warfarin, your healthcare provider should do blood tests regularly to check how fast your blood clots, during treatment with Gefisa®.

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

Missed dose
If you miss a dose of Gefisa®, take it as soon as you remember. If it is less than 12 hours until your next dose, skip the missed dose. Take your next dose at your regular time.

Overdose
If you take too much Gefisa® call your healthcare provider or go to the nearest hospital emergency room right away.

Pregnancy and lactation
It is forbidden to take Gefisa® during pregnancy and breast-feeding. Females who are able to become pregnant should use an effective method of birth control during treatment with Gefisa® and for at least 2 weeks after the last dose of Gefisa®. You should avoid becoming pregnant during treatment with Gefisa®. Tell your healthcare provider right away if you become pregnant during treatment with Gefisa®.

It is not known if Gefisa® passes into human milk. Do not breastfeed during treatment with Gefisa®.

Fertility: Gefisa® may cause fertility problems in females. Talk to your healthcare provider if you plan to become pregnant.

Patient information
- Take Gefisa® exactly as your healthcare provider tells you to take it.
- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with Gefisa® if you have side effects.
- Take Gefisa® 1 time each day.
- You can take Gefisa® with or without food.
- **If you cannot swallow Gefisa® tablets whole:**
  - o place your dose of Gefisa® in a container with 4 to 8 ounces (120-240 CC) of water and stir for about 15 minutes
  - o drink the mixture right away
  - o place another 4 to 8 ounces of water in the same container, and drink it right away

Storage
- Keep away from light and moisture. Store below 30°C.
- Keep out of the reach of children.
- Keep the desiccant in the bottle.
- Safely throw away medicine that is out of date or that you no longer need.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging
- Bottle of 30 F. C. Tablets.

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