SebErb

Gefitinib INN 250 mg Tablet

"Please carefully read the full leaflet"

COMPOSITION
SebErb tablet: Each Film coated tablet contains Gefitinib INN 250 mg.

DESCRIPTION
SebErb (Gefitinib) is a quinozolamine tyrosine kinase inhibitor. The chemical name of Gefitinib is 4-Quinazolin-amine N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholin) propoxy.

PHARMACEUTICAL FORM AND STRENGTH
SebErb (Gefitinib) is available as 250 mg film coated tablet for oral administration.

THERAPEUTIC INDICATIONS
SebErb (Gefitinib) is 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.

DOSAGE AND ADMINISTRATION
Recommended dose for SebErb (Gefitinib) is 250 mg orally, once daily with or without food.

CLINICAL PHARMACOLOGY
MECHANISM OF ACTION
Gefitinib reversibly inhibits the intracellular phosphorylation of numerous tyrosine kinases associated with transmembrane cell surface receptors, including the tyrosine kinases associated with the epidermal growth factor receptor (EGFR-TK). EGFR is expressed on the cell surface of many normal cells and cancer cells.

PHARMACOKINETICS
Absorption and Distribution
Gefitinib is slowly absorbed, with peak plasma levels occurring 3-7 hours after dosing and mean oral bioavailability of 60%. Bioavailability is not significantly altered by food. Gefitinib is extensively distributed throughout the body with a mean steady state volume of distribution of 1400 L following intravenous administration. In vitro binding of Gefitinib to human plasma proteins (serum albumin and α1-acid glycoprotein) is 90% and is independent of drug concentrations.

Metabolism and Elimination
Gefitinib undergoes extensive hepatic metabolism in humans, predominantly by CYP3A4. Three sites of biotransformation have been identified: metabolism of the Npropoxymorpholino-group, demethylation of the methoxy-substituent on the Quinazoline, and oxidative defluorination of the halogenated phenyl group.
Five metabolites were identified in human plasma. Only O-desmethyl Gefitinib has exposure comparable to Gefitinib. Although this metabolite has similar EGFR-TK activity to Gefitinib in the isolated enzyme assay, it had only 1/14 of the potency of Gefitinib in one of the cell based assays.
Gefitinib is cleared primarily by the liver, with total plasma clearance and elimination half-life values of 595 mL/min and 48 hours, respectively, after intravenous administration. Excretion is predominantly via the feces (86%), with renal elimination of drug and metabolites accounting for less than 4% of the administered dose.

CONTRAINDICATION
May cause hypersensitivity to active substance or to any of the excipients.

USE IN SPECIFIC POPULATION
Pregnancy: Pregnancy category C.
This drug should not be used during pregnancy unless clearly needed as it can cause fetal harm based on its mechanism of action
Nursing mothers: Mother should be advised against breast feeding while receiving Gefitinib.
Pediatric Use: The safety and effectiveness of Gefitinib in pediatric patients have not been established.
Geriatric Use: No overall differences in safety or efficacy were observed between subjects 65 years and older and younger than 65.

SIDE EFFECTS
The most common side effects were dry skin itching, rash, acne, mouth sore, weakness, diarrhea, anorexia weight loss.

WARNINGS AND PRECAUTIONS
1. Interstitial lung disease (ILD): ILD occurred in patients taking Gefitinib. Should be Withheld Gefitinib for worsening of respiratory symptoms. Need discontinue Gefitinib if ILD is confirmed.
2. Hepatotoxicity: Should be withheld Gefitinib for Grade 2 or higher for ALT and/or AST elevations. Should discontinue for severe hepatic impairment.
3. Gastrointestinal perforation: Discontinue Gefitinib for gastrointestinal perforation.
4. Diarrhea: Withhold Gefitinib for Grade 3 or higher diarrhea.
5. Ocular Disorders including Keratitis: For signs and symptoms of severe or worsening ocular disorders including keratitis Gefitinib should be withheld.
6. Bullous and Exfoliative Skin Disorders: For Grade 3 or higher skin reactions or exfoliative conditions Gefitinib need to discontinue.
7. Embryo-fetal Toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception.

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

DRUG INTERACTIONS
• CYP3A4 Inducer: Gefitinib dose needs to be increased to 500 mg daily in patients receiving a strong CYP3A4 inducer.
• CYP3A4 Inhibitor: Adverse reactions should be monitored if concomitant use with Gefitinib.
• Drugs Affecting Gastric pH: Concomitant use of Gefitinib Should be avoided with proton pump inhibitors, if possible.
• Hemorrhage in patients taking warfarin: Changes in prothrombin time or INR should be monitored.

OVERDOSE
There is no specific treatment indicated for Gefitinib overdosing. So in case of suspected overdose Gefitinib should be withheld, instituted for supportive care and observe until clinical stabilization.

PHARMACEUTICAL INFORMATIONS
Storage Conditions
Store below 25° C.
Store in a cool and dry place.
Keep away from light.
Keep out of the reach of children.

How Supplied
SebErb Tablet: Each commercial box contains 1x7's, 1x10's, 2x7's, 2x 10's and 3x10's tablets in Alu-Alu blister pack.

Manufactured By

genvio

Genvio Pharma Limited.
Trishal, Mymensingh-2220, Bangladesh
www.genvio.com.bd