Signera™

Neratinib Maleate INN

Jenphar Bangladesh | جنفار بنغلاديش

Composition:

Signera™ 40 mg Tablet: Each Film coated tablet contains Neratinib Maleate INN equivalent to Neratinib 40 mg.

Pharmacology:

Neratinib is a kinase inhibitor that irreversibly binds to Epidermal Growth Factor Receptor (EGFR), Human Epidermal Growth Factor Receptor 2 (HER2), and HER4. In vitro, Neratinib reduces EGFR and HER2 autophosphorylation, downstream MAPK and AKT signaling pathways and showed antitumor activity in EGFR and/or HER2 expressing carcinoma cell lines.

Indications:

Extended Adjuvant Treatment of Early-Stage Breast Cancer:

Neratinib as a single agent is indicated for the extended adjuvant treatment of adult patients with early-stage human epidermal growth factor receptor 2 (HER2)-positive breast cancer, to follow adjuvant trastuzumab based therapy.

Advanced or Metastatic Breast Cancer:

Neratinib in combination with capecitabine is indicated for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

Dosage and Administration:

Extended adjuvant treatment of early-stage breast cancer:

The recommended dose of Neratinib is 240 mg (6 tablets) given orally once daily with food, continuously until disease recurrence for up to one year.

Advanced or metastatic breast cancer:

The recommended dose of Neratinib is 240 mg (6 tablets) given orally once daily with food on Days 1–21 of a 21-day cycle plus capecitabine (750 mg/m^2 given orally twice daily) on Days 1–14 of a 21-day cycle until disease progression or unacceptable toxicities.

Neratinib monotherapy dose modifications for adverse reactions:

Dose Level	Neratinib Dose
Recommended starting dose	240 mg daily
First dose reduction	200 mg daily
Second dose reduction	160 mg daily
Third dose reduction	120 mg daily

Contraindications:

None.

Adverse Reaction:

The most common adverse reactions (reported in ≥5% of patients) were:

- Neratinib as a single agent: Diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increased, nail disorder, dry skin, abdominal distention, epistaxis, weight decreased and urinary tract infection.
- Neratinib in combination with capecitabine: Diarrhea, nausea, vomiting, decreased appetite, constipation, fatigue/asthenia, weight decreased, dizziness, back pain, arthralgia, urinary tract infection, upper respiratory tract infection, abdominal distention, renal impairment and muscle spasms.

Warning and Precautions:

Diarrhea: Manage diarrhea through either Neratinib dose escalation or loperamide prophylaxis. If diarrhea occurs despite recommended prophylaxis, treat with additional antidiarrheal, fluids and electrolytes as clinically indicated. Withhold Neratinib in patients experiencing severe or persistent diarrhea. Permanently discontinue Neratinib in patients experiencing Grade 4 diarrhea or Grade ≥2 diarrhea that occurs after maximal dose reduction.

Hepatotoxicity: Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated. Withhold Neratinib in patients experiencing Grade 3 liver abnormalities and permanently discontinue Neratinib in patients experiencing Grade 4 liver abnormalities.

Embryo-Fetal Toxicity: Neratinib can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

Use in Specific Populations:

Pregnancy: Neratinib can cause embryo-fetal harm when administered to a pregnant woman. There are no available data on Neratinib use in pregnant women.

Lactation: No data are available regarding the presence of Neratinib or its metabolites in human milk or its effects on the breastfed infant or on milk production. Advise lactating women not to breastfeed while taking Neratinib and for at least 1 month after the last dose.

Females and Males of Reproductive Potential: Advise females of reproductive potential to use effective contraception during treatment with Neratinib and for at least 1 month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of Neratinib.

Pediatric Use: The safety and efficacy of Neratinib in pediatric patients has not been established.

Geriatric Use: There was a higher frequency of treatment discontinuations due to adverse reactions in the ≥ 65 years age group than in the < 65 years age group. No overall differences in effectiveness were observed between patients ≥65 years old and patients <65 years old.

Hepatic Impairment: No dosage modifications are recommended for patients with mild to moderate hepatic impairment (Child Pugh A or B). Patients with severe, pre-existing hepatic impairment (Child Pugh Class C), reduce the Neratinib dosage for patients.

Drug Interaction:

Gastric acid reducing agents: Concomitant use of Neratinib with a proton pump inhibitor (PPI), H2-receptor antagonist, or antacid may reduce Neratinib activity. Avoid concomitant use with proton pump inhibitors. Separate Neratinib by at least 2 hours before or 10 hours after H2-receptor antagonists. Or separate Neratinib by at least 3 hours after antacids.

Strong CYP3A4 inhibitors: Concomitant use of Neratinib with a strong CYP3A4 inhibitor increased Neratinib activity, which may increase the risk of Neratinib toxicity. Avoid concomitant use of Neratinib with strong CYP3A4 inhibitors.

P-gp and moderate CYP3A4 dual inhibitors: Concomitant use of Neratinib with a P-gp and moderate CYP3A4 dual inhibitor which may increase the risk of Neratinib toxicity. Avoid concomitant use of Neratinib with P-gp and moderate CYP3A4 dual inhibitors.

Strong or moderate CYP3A4 inducers: Concomitant use of Neratinib with a strong CYP3A4 inducer may reduce Neratinib activity. Avoid concomitant use of Neratinib with strong or moderate CYP3A4 inducers.

Certain P-gp substrates: Monitor for adverse reactions of P-gp substrates for which minimal concentration change may lead to serious adverse reactions when used concomitantly with Neratinib

Overdose:

There is no specific antidote, and the benefit of hemodialysis in the treatment of Neratinib overdose is unknown. In the event of an overdose, administration should be withheld and general supportive measures undertaken.

Storage Condition:

Store in a cool and dry place below 30° C, protect from light. Keep out of the reach of children.

Packaging:

Signera™ 40 mg Tablet: Each box contains 28 tablets and one packet silica gel in a sealed HDPE container.

Manufactured by:

Jenphar Bangladesh Ltd.

Sreepur, Gazipur, Bangladesh.

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