Nerlynx (neratinib)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Nerlynx
- **Generic name:** Neratinib
- **Pharmacological class:** Kinase inhibitor
- **Strength and Formulation:** 40mg; tabs
- **Manufacturer:** Puma Biotechnology
- **How supplied:** Tabs—126,180
- **Legal Classification:** Rx

NERLYNX


NDC 70437-240-18
nerlynx™
(neratinib) tablets
40 mg
Each film-coated tablet contains 40 mg neratinib
equivalent to 48.31 mg neratinib maleate
180 tablets
Rx only
NDC 70437-240-18
nerlynx™
(neratinib) tablets
40 mg
Rx only
180 tablets
W104

Indications

- Extended adjuvant treatment of **early stage HER2-overexpressed/amplified breast cancer** following adjuvant trastuzumab-based therapy

Dosage & Administration

- Initiate **antidiarrheal prophylaxis** (loperamide) with the first dose and continue during the first 2 treatment cycles (56 days); see full labeling
- Swallow whole and take with food
- 240mg once daily for 1 year
- **Severe hepatic impairment** (Child-Pugh C): reduce initial dose to 80mg

Dosage & Administration

- **Dose modifications for adverse reactions**:
  - First dose reduction: 200mg/day
  - Second dose reduction: 160mg/day
  - Third dose reduction: 120mg/day
  - Discontinue if unable to tolerate 120mg/day
- Dose modifications for diarrhea, hepatotoxicity, or other general toxicities: see full labeling

Considerations for Special Populations

- **Pregnancy:** Exclude status prior to initiation
- **Nursing mothers:** Not recommended during and for at least 1 month after last dose
- **Pediatric:** Not established
- **Hepatic impairment:** Severe hepatic impairment: reduce dose

Warnings/Precautions

- Monitor and treat **diarrhea** as needed; interrupt and reduce subsequent doses if severe diarrhea with dehydration occurs
- Perform **stool cultures** as clinically indicated to exclude infectious causes of Grade 3/4 or any grade of diarrhea with complications

Warnings/Precautions

- Measure **total bilirubin, AST/ALT, alkaline phosphatase** prior to initiation, monthly for the first 3 months, then every 3 months during treatment and as clinically indicated
- Embryo-fetal toxicity
- Use effective contraception during therapy and for at least 1 month (females) or 3 months (males) after last dose

Interactions

- **Avoid** concomitant PPIs, H_2-receptor antagonists, strong or moderate CYP3A4 inhibitors (eg, clarithromycin, grapefruit juice, ketoconazole, ciprofloxacin, others), and strong or moderate CYP3A4 inducers (eg, carbamazepine, phenytoin, rifampin, St. John’s wort, others)

Interactions

- Separate dosing by 3hrs after **antacids**
- Increased **cardiotoxicity** risk with digoxin
- May inhibit transport of P-gp substrates (eg, dabigatran, fexofenadine)

Adverse Reactions

- Diarrhea
- Nausea
- Abdominal pain
- Fatigue
- Vomiting
- Rash
- Stomatitis
- Decreased appetite
- Muscle spasms
- Dyspepsia
- AST/ALT increase
- Nail disorder
- Dry skin
- Abdominal distention
- Weight decreased
- Urinary tract infection
- Hepatotoxicity

Mechanism of Action

- Neratinib is a **kinase inhibitor** that irreversibly binds to epidermal growth factor receptor (EGFR), human epidermal growth factor receptor 2 (HER2), and HER4
- *In vivo*, oral administration resulted in inhibition of tumor growth in models with tumor cell lines expressing HER2 and EGFR

Clinical Studies

- Nerlynx was studied in a multicenter, randomized, double-blind, placebo-controlled trial (N=2,840), **ExteNET**, after adjuvant treatment with trastuzumab
- Female patients with early stage HER2-positive breast cancer were randomized to either Nerlynx 240mg (N=1,420) or placebo(N=1,420)

Clinical Studies

- The major efficacy outcome measure was **invasive disease free survival (iDFS),** defined as the time between the date of randomization to the first occurrence of invasive recurrence, distant recurrence, or all-cause mortality with 2 years and 28 days of follow-up

Clinical Studies

- Treatment with Nerlynx was more effective vs. placebo at 24 months
  - iDFS was **94.2%** in Nerlynx arm vs. **91.9%** in placebo arm
  - Hazard ratio (HR) 0.66 (95% CI: 0.49, 0.90; *P*<0.008)

Clinical Studies

- About 75% of patients were re-consented for extended follow-up beyond 24 months
- The exploratory analysis suggests that the iDFS results at 5 years are consistent with the 2-year iDFS results seen in ExteNET

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/nerlynx/drug/34720/