INVITATION

EXTEND HER Protection in HER2+ Early Breast Cancer

FRIDAY 17th JUNE 2022 13:15 – 14:00

Oncology Forum - Meeting Room 2A, LEVEL 3

Prof Daniel Rea, University of Birmingham

Dr Medy Tsalic, Queen Elizabeth Hospital Birmingham

- CLINICAL RISK FACTORS IN HER2+ EARLY BREAST CANCER AND UNMET NEEDS
- NERLYNX▼ (NERATINIB) IN THE HER2+ EARLY BREAST CANCER PATHWAY
- EFFECTIVE PATIENT MANAGEMENT & TREATMENT COMPLETION

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UK/NER/0444 | June 2022

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Nerlynx (neratinib) ▼Great Britain (GB) Prescribing Information

(Please refer to Nerlynx Summary of Product Characteristics (SmPC) for full Prescribing Information)

Presentation Each film-coated tablet contains neratinib maleate, equivalent to 40 mg neratinib. **Indication** Nerlynx is indicated for the extended adjuvant treatment of adult patients with early-stage hormone receptor positive HER2-overexpressed/amplified breast cancer and who completed adjuvant trastuzumab-based therapy less than one year ago. **Dosage and administration** 240 mg (six 40 mg tablets) taken orally once daily, continuously for one year. The tablets should be swallowed whole preferably with water, should not be crushed or dissolved and should be taken with food, preferably in the morning. Patients should initiate treatment within 1 year after completion of trastuzumab therapy. *Dose modification:* Management of some adverse reactions may require dose interruption and/or dose reduction or treatment discontinuation. First dose reduction 200mg daily, second dose reduction 160mg daily, third dose reduction 120mg daily. Guidelines for the dose modifications in relation to diarrhoea management are shown in Table 3 of the SmPC. Neratinib should be discontinued in the following situations: if patient fails to recover to Grade 0 to 1 from treatment-related toxicity; for toxicities that result in a treatment delay > 3 weeks; for patients that are unable to tolerate 120 mg daily; Grade 4 toxicity. Please see the SmPC for full details. *Elderly:* No dose adjustment is required. There is no data in patients ≥85 years. *Paediatrics:* There is no relevant use of neratinib in the paediatric population in the indication breast cancer. **Contraindications** Hypersensitivity to the active substance or to any of the excipients. Co-administration with strong CYP3A4/P-gp inducers, such as: carbamazepine, phenytoin, St John's wort, rifampicin. Severe hepatic impairment (Child-Pugh C). **Special Warnings and Precautions** *Diarrhoea:* Severe diarrhoea and associated dehydration can occur with neratinib treatment. Initiate prophylactic treatment with an anti-diarrhoeal with the first dose of neratinib and maintain regular dosing of the anti-diarrhoeal during the first 1-2 months of treatment, titrating to 1-2 bowel movements per day (refer to SmPC for further information). *Elderly* (≥65 years) should be monitored because they are at a higher risk of renal insufficiency and dehydration. Significant chronic gastrointestinal disorder with diarrhoea as a major symptom: These patients should be carefully monitored. *Renal impairment:* These patients should be carefully monitored since they are at higher risk of dehydration if they develop diarrhoea. *Liver function*: Hepatotoxicity has been reported in patients treated with neratinib. Liver function tests should be monitored at 1 week, then monthly for the first 3 months and every 6 weeks thereafter while on treatment or as clinically indicated. Patients who experience ≥ Grade 3 diarrhoea requiring IV fluid treatment or any signs or symptoms of hepatotoxicity, should be evaluated for changes in liver function tests. Fractionated bilirubin and prothrombin time should also be collected during hepatotoxicity evaluation. *Left ventricular function*: Left ventricular dysfunction (LVD) has been associated with HER2 inhibition. In patients with known cardiac risk factors, conduct cardiac monitoring, including assessment of Left Ventricular Ejection Fraction (LVEF), as clinically indicated. *Proton pump inhibitors (PPIs), H2-receptor antagonists and antacids*: Treatments that increase gastrointestinal pH may lower the absorption of neratinib, thus decreasing systemic exposure. Co-administration with PPIs is not recommended. In case of H_2-receptor antagonists, Nerlynx should be taken at least 2 hours before or 10 hours after the intake of the H_2-receptor antagonist. Separate dosing of Nerlynx and antacids by at least three hours (see SmPC Section 4.2, Section 4.5 and Section 5.2). *Skin and subcutaneous tissue disorders*: Neratinib is associated with skin and subcutaneous tissue disorders. Patients with symptomatic skin and subcutaneous tissue disorders should be carefully monitored. *Concomitant treatment with inhibitors of CYP3A4/P-gp*: Concomitant treatment with strong or moderate CYP3A4/P-gp inhibitors is not recommended due to risk of increased exposure to neratinib. If the inhibitor cannot be avoided, reduce Nerlynx dose to 40 mg (one 40 mg tablet) taken once daily with a strong CYP3A4/P-gp inhibitor. For moderate CYP3A4/P-gp inhibitors reduce dose to 40 mg (one tablet) taken once daily. If well tolerated, increase to 80 mg for at least 1 week, then to 120 mg for at least 1 week, and to 160 mg as a maximal daily dose. Patient should be monitored carefully. After discontinuation of a strong or moderate CYP3A4/P-gp inhibitor, resume previous dose of Nerlynx 240 mg. Grapefruit or pomegranate/grapefruit or pomegranate juice should be avoided during treatment with neratinib. *Concomitant treatment with moderate inducers of CYP3A4 and P-gp*: Concomitant treatment with moderate CYP3A4 and P-gp inducers is not recommended as it may lead to a loss of neratinib efficacy. **Interactions** (refer to SmPC for full list of interactions). Neratinib is primarily metabolised by CYP3A4 and is a P-gp substrate. Co-administration of neratinib with Breast Cancer Resistance Protein (BCRP) substrates (e.g., rosuvastatin, sulfasalazine and irinotecan) may lead to an increase in their exposure. Patients who are treated with BCRP substrates should be monitored carefully. Neratinib is an inhibitor of P-glycoprotein (P-gp) efflux transporters. Therefore, concomitant use with therapeutic agents with a narrow therapeutic window whose absorption involves P-gp transporters in the gastrointestinal tract should be carefully monitored. **Pregnancy and Lactation** *Women of Childbearing potential/contraception*: Women must use highly effective contraceptive measures while taking neratinib and for 1 month after stopping treatment. Women using systemically acting hormonal contraceptives should use a barrier method. Men should use a barrier method of contraception during treatment and for 3 months after stopping treatment. *Pregnancy*: Neratinib may cause foetal harm if administered to pregnant women. *Breast-feeding*: It is not known if neratinib is excreted in human milk. **Undesirable effects** Please refer to the Nerlynx SmPC before prescribing. *Very Common* (≥1/10) Decreased appetite, diarrhoea, vomiting, nausea, abdominal pain, abdominal pain upper, stomatitis, rash, muscle spasms, fatigue. *Common* (≥ 1/100 to < 1/10) Urinary tract infection, dehydration, epistaxis, abdominal distension, dry mouth, dyspepsia, alanine aminotransferase increased, aspartate aminotransferase increased, nail disorder, skin fissures, dry skin, blood creatinine increased, syncope, weight decreased. *Uncommon* (≥1/1,000 to < 1/100) Blood bilirubin increased, renal failure. **Driving and operating machinery** Neratinib has minor or moderate influence on the ability to drive and use machines. The clinical status of the patient should be considered when assessing the patient's ability to drive and use machinery. **Overdose** Administration should be withheld and general supportive measures undertaken. **Legal category**: POM. **Marketing authorisation holder** Pierre Fabre Limited, 250 Longwater Avenue, Green Park, Reading, Berkshire, RG2 6GP, UK. **Package quantity, Marketing Authorisation number and basic NHS price** Nerlynx 40mg x 180 tablets (30 days treatment) £4500. PLGB 00603/0246. Further information is available on request from Medical Information at Pierre Fabre Limited, 250 Longwater Avenue, Green Park, Reading, Berkshire, RG2 6GP. Email: UK_MI@pierre-fabre.com. Tel: 0800 085 5292. **Date of Review**: April 2022. UK/NER/0416

Adverse events should be reported. In the UK reporting forms and information can be found at the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in Google Play or Apple App Store.

Adverse events should also be reported to Pierre Fabre Ltd. Telephone: United Kingdom 0800 0855 292 or by email at: UK_MI@pierre-fabre.com

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Nerlynx (neratinib) ▼Northern Ireland (NI) & Republic of Ireland (ROI) Prescribing Information

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In the Republic of Ireland adverse events should be reported to the HPRA. Reporting information for the HPRA can be found on the HPRA website: www.hpra.ie

Adverse events should also be reported to Pierre Fabre Ltd. Telephone: Northern Ireland: 0800 0855 292 Republic of Ireland 1800 812 464 or by email at: UK_MI@pierre-fabre.com or IE_MI@pierre-fabre.com

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