Clinical Policy: Neratinib (Nerlynx)

Reference Number: PA.CP.PHAR.365
Effective Date: 10.17.18
Last Review Date: 10.17.18

Revision Log

Description
Neratinib (Nerlynx®) is a kinase inhibitor that irreversibly binds to epidermal growth factor receptor, human epidermal growth factor receptor 2 (HER2), and HER4.

FDA Approved Indication
Nerlynx is indicated for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab-based therapy.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Nerlynx is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (member meets all)**:**

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Disease is HER2-positive;
4. Member meets one of the following (a or b):
   a. Both (i and ii):
      i. Documentation of previous adjuvant treatment with trastuzumab;
      ii. Disease is early stage (stage 1-3) or hormone-receptor positive;
   b. Prescribed in combination with capecitabine for recurrent brain metastases (off-label);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg per day (6 tablets per day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Breast Cancer (member meets all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 240 mg per day (6 tablets per day);
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (member meets 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER: human epidermal growth factor receptor
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Herceptin® (trastuzumab) Ogivri™ (trastuzumab-dkst)	• Initial dose of 4 mg/kg IV, then 2 mg/kg IV weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin). One week after the last weekly dose, administer 6 mg/kg IV every 3 weeks to complete a total of 52 weeks of therapy OR • Initial dose of 8 mg/kg IV, then 6 mg/kg IV every 3 weeks for 52 weeks	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- Per the Nerlynx prescribing information, antidiarrheal prophylaxis is recommended during the first 2 cycles (56 days) of Nerlynx treatment and should be initiated with the first dose of Nerlynx in order to address the risk of treatment discontinuation due to diarrhea, as was seen in the pivotal ExteNET trial.
- Nerlynx is FDA-approved for a one year total duration of therapy as it was only administered for one year in the pivotal ExteNET trial; however, the NCCN does not recommend any specific length of treatment.
- The NCCN recommends Nerlynx for hormone receptor-positive, HER2-positive breast cancer in patients with a perceived high risk of recurrence. Nerlynx is also recommended for the treatment of recurrent brain metastases in patients with breast cancer in combination with capecitabine (category 2A) or paclitaxel (category 2B).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	240 mg PO QD	240 mg/day

VI. Product Availability
Tablet: 40 mg

VII. References
1. Nerlynx Prescribing Information. Los Angeles, CA: Puma Biotechnology, Inc.; July 2017. Available at: www.nerlynx.com. Accessed July 6, 2018.
2. National Comprehensive Cancer Network. Breast Cancer Version 1.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 5, 2018.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 5, 2018.
4. National Comprehensive Cancer Network. Central Nervous System Cancers Version 1.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed July 6, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/18	