envolve Pharmacy Solutions

Clinical Policy: Neratinib (Nerlynx)

Reference Number: ERX.SPA.219
Effective Date: 09.05.17
Last Review Date: 11.18 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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(s)
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 Envolve Pharmacy Solutions™ that Nerlynx is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is HER2-positive;
5. 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);
6. 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: Length of Benefit

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Breast Cancer (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Nerlynx for breast cancer and has received this medication for at least 30 days;
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: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 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
- Contraindication(s): none reported
- Boxed warning(s): 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
Tablets: 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	09.05.17	11.17
4Q 2018 annual review: added NCCN off-label uses; added specialist involvement in care; removed restriction for only 1 year of total therapy as NCCN does not recommend a specific duration of use; modified approval durations to length of benefit; references reviewed and updated.	07.06.18	11.18

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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