Clinical Policy: Neratinib (Nerlynx)

Reference Number: ERX.SPA.219
Effective Date: 12.01.17
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

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:

- As a single agent, for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer, to follow adjuvant trastuzumab-based therapy.
- In combination with capecitabine, 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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

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, b, or c):
   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, advanced, or metastatic disease, and member has received two or more prior anti-HER2 based regimens used in the metastatic setting;
   c. Prescribed in combination with capecitabine for central nervous system brain metastases;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg (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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

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 (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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

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) Ontruzant® (Trastuzumab-dttb) Herzuma® (Trastuzumab-pkrb) Trazimera™ (Trastuzumab-qyyp)	Administer according to one of the following doses and schedules for a total of 52 weeks: ***Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:*** During and following paclitaxel, docetaxel, or docetaxel/carboplatin: • Initial dose of 4 mg/kg as an IV infusion over 90 minutes then at 2 mg/kg as an IV infusion over 30 minutes weekly during chemotherapy for the first 12 weeks (paclitaxel or docetaxel) or 18 weeks (docetaxel/carboplatin). • One week following the last weekly dose of the trastuzumab product, administer trastuzumab product	8 mg/kg

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Kanjinti™ (Trastuzumab-anns)	at 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks. ***Herceptin, Ogivri, Ontruzant, Trazimera, Kanjinti:*** As a single agent within 3 weeks following completion of multi-modality, anthracycline based chemotherapy regimens: • Initial dose: 8 mg/kg as an IV infusion over 90 minutes. • Subsequent doses: 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks	
Herceptin Hylecta™ (Trastuzumab-hyaluronidase-oysk)	***Herceptin Hylecta (subcutaneous product):*** As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; as part of a treatment regimen with docetaxel and carboplatin; as a single agent following multi-modality anthracycline based therapy: 600 mg trastuzumab and 10,000 units hyaluronidase administered subcutaneously over approximately 2-5 minutes once every 3 weeks	600 mg/10,000 units every 3 weeks
Perjeta® (pertuzumab)	Initial 840 mg IV followed by a maintenance dose of 420 mg IV every 3 weeks in combination with trastuzumab and either docetaxel or paclitaxel	Maintenance: 420 mg every 3 weeks
Kadcyla® (ado-trastuzumab emtansine)	3.6 mg/kg IV every 3 weeks	3.6 mg/kg every 3 weeks
Enhertu® (fam-trastuzumab deruxtecan-nxki)	5.4 mg/kg once every 3 weeks	5.4 mg/kg every 3 weeks

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 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.

V. Dosage and Administration

Indication	Dosing Regimen*	Maximum Dose
Breast cancer extended adjuvant treatment	240 mg PO QD	240 mg/day
Breast cancer advanced, recurrent, or metastatic disease	240 mg PO QD on days 1-21 plus capecitabine 750 mg/m^2 PO BID on days 1-14 of a 21-day cycle	240 mg/day

**A two-week dose escalation may be considered instead of starting at the 240 mg daily dose for patients with early-stage breast cancer and metastatic breast cancer: week 1 (days 1-7): 120 mg PO QD; week 2 (days 8-14): 160 mg PO QD.*

VI. Product Availability
Tablet: 40 mg

VII. References

1. Nerlynx Prescribing Information. Los Angeles, CA: Puma Biotechnology, Inc.; March 2022. Available at: www.nerlynx.com. Accessed July 29, 2022.
2. National Comprehensive Cancer Network. Breast Cancer Version 4.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 29, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 29, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
4Q 2019 annual review: removed off-label capecitabine combination use from criteria (NCCN category 2B); added new trastuzumab biosimilars (Ontruzant, Herzuma, Trazimera, and Kanjinti) to Appendix B therapeutic alternatives; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	08.12.19	11.19
RT2: added new indication for use in combination with capecitabine for advanced, recurrent, or metastatic breast cancer.	04.07.20	05.20
Added NCCN Compendium supported use in combination with capecitabine for CNS metastases; references reviewed and updated.	05.20.20	08.20
4Q 2020 annual review: no significant changes; references reviewed and updated.	07.15.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	08.11.21	11.21
4Q 2022 annual review: no significant changes; references reviewed and updated.	07.29.22	11.22

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.