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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	July 28, 2017
Subject:	Nerlynx	**Page:**	1 of 4

Last Review Date: March 7, 2025

Nerlynx

Description

Nerlynx (neratinib)

Background
Nerlynx (neratinib) is a tyrosine kinase inhibitor that irreversibly binds to epidermal growth factors, human epidermal growth factor 2 (HER2) and HER4. Nerlynx (neratinib) is clinically approved to be used in patients with HER2 protein positive breast cancer. Nerlynx effects have been shown to reduce risk of breast cancer recurrence (1).

Regulatory Status
FDA-approved indications: Nerlynx is a kinase inhibitor indicated: (1)

- 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

Safety and effectiveness in pediatric patients have not been established (1).

Related policies
Enhertu, Herceptin Hylecta, Kadcyla, Margenza, Perjeta, Phesgo, Trastuzumab, Tukysa, Tykerb

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Nerlynx may be considered **medically necessary** if the conditions indicated below are met.

Nerlynx may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Early stage breast cancer (Stage 1 – 3c)
    a. Used for extended adjuvant treatment
    b. Previously treated with trastuzumab
2. Advanced or Metastatic breast cancer (Stage 4)
    a. Used in combination with capecitabine
    b. Patient has previously received two or more anti-HER2 based regimens

AND ALL of the following:

1. Human epidermal growth factor receptor 2 (HER2)-positive
2. Prescriber agrees to manage diarrhea through **ONE** of the following:
    a. Nerlynx dose escalation with antidiarrheal treatment as needed
    b. Antidiarrheal prophylaxis starting with the first dose of Nerlynx and continuing during the first 56 days of treatment and as needed thereafter

Prior – Approval *Renewal* Requirements

NO renewal for early stage breast cancer

Age 18 years of age or older

Diagnosis

Patient must have the following:

Advanced or metastatic breast cancer (Stage 4)

AND ALL of the following:

1. Used in combination with capecitabine
2. **NO** disease progression or unacceptable toxicity

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Quantity 540 tablets per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity 540 tablets per 90 days

Duration 12 months

NO renewal for early stage breast cancer

Rationale

Summary

Nerlynx (neratinib) is a tyrosine kinase inhibitor that irreversibly binds to epidermal growth factors, human epidermal growth factor 2 (HER2) and HER4. Nerlynx (neratinib) is clinically approved to be used in patients with HER2 protein positive breast cancer. The safety and effectiveness in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Nerlynx while maintaining optimal therapeutic outcomes.

References

1. Nerlynx [package insert]. Los Angeles, CA: Puma Biotechnology, Inc.; March 2022.

2. NCCN Drugs & Biologics Compendium® Neratinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.

Policy History

Date	Action
July 2017	Addition to PA
September 2017	Annual review
December 2017	Annual editorial review Addition of the requirement for the prescriber agreeing to initiate antidiarrheal prophylaxis with the first dose and continue during the first 2 cycles (56 days) of treatment and as needed thereafter per SME. Removal of renewal section per SME
March 2018	Annual review
June 2019	Annual review and reference update
March 2020	Addition of indication: advanced or metastatic breast cancer and added quantity limit of 540 tablets per 90 days
June 2020	Annual review
September 2020	Annual review
December 2020	Annual review and reference update
June 2021	Annual review and reference update
July 2021	Revised antidiarrheal requirement to give providers the option to dose escalate and manage diarrhea as needed
September 2021	Annual review and reference update
July 2022	Per reconsideration review: Specify early stage breast cancer is for adjuvant treatment and combine the advanced and metastatic indications on initiation for parity with continuation. Added staging to diagnoses per PI
September 2022	Annual review and reference update
June 2023	Annual review and reference update
March 2024	Annual review and reference update
June 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.