UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 1226-10
Program	Prior Authorization/Notification
Medication	Nerlynx® (neratinib)
P&T Approval Date	9/2017, 9/2018, 9/2019, 4/2020, 5/2021, 5/2022, 5/2023, 7/2023, 7/2024, 7/2025
Effective Date	10/1/2025

1. Background:

Nerlynx® (neratinib) is a kinase inhibitor indicated as a single agent, for the extended adjuvant treatment of adult patients with early-stage human epidermal growth factor receptor 2 (HER2)-positive breast cancer, to follow adjuvant trastuzumab-based therapy. It is also indicated 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.

The National Comprehensive Cancer Network (NCCN) recommends the use of Nerlynx as extended adjuvant therapy following adjuvant trastuzumab-containing therapy in hormone receptor (HR)-positive, HER2-positive patients with a perceived high risk of recurrence and node positive breast cancer, as fourth-line therapy and beyond in combination with capecitabine for recurrent unresectable or stage IV (M1) HER2-positive breast cancer, and for stage IV (M1) breast cancer as a single agent, or in combination with fulvestrant with or without trastuzumab for HR-positive, HER2-negative disease in patients who have already received a CDK4/6 inhibitor therapy or for triple negative disease. NCCN also recommends the use of Nerlynx in combination with capecitabine or paclitaxel as treatment for brain metastases in HER2 positive breast cancer and as second-line or subsequent therapy for HER2 positive cervical cancer.

Coverage Information:
Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. <u>Patients less than 19 years of age</u>

1. **Nerlynx** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. <u>Early-Stage or Node-Positive Breast Cancer</u>

1. **Nerlynx** will be approved based on **one** of the following criteria:

   a. **All** of the following:

      (1) Diagnosis of early-stage breast cancer

      -AND-

      (2) Disease is human epidermal growth factor receptor 2 (HER2)-positive

      -AND-

      (3) Used as extended adjuvant therapy following adjuvant trastuzumab-containing therapy (e.g., Herceptin®, Kanjinti™)

      -OR-

   b. **All** of the following:

      (1) Diagnosis of node positive breast cancer

      -AND-

      (2) Disease is hormone receptor (HR)-positive and HER2-positive

      -AND-

      (3) Used as extended adjuvant therapy following adjuvant trastuzumab-containing therapy (e.g., Herceptin®, Kanjinti™)

      -AND-

      (4) Patient has a perceived high risk of recurrence

   Authorization will be issued for 12 months. Duration of coverage is limited to 12 months per occurrence.

C. Advanced or Metastatic Breast Cancer

1. **Initial Authorization**

   a. **Nerlynx** will be approved based on **one** of the following criteria:

      (1) All of the following:

         (a) Diagnosis of advanced or metastatic breast cancer

-AND-

(b) Disease is HER2-positive

-AND-

(c) Patient has received two or more prior anti-HER2 based regimens in metastatic setting

-AND-

(d) Will be used in combination with capecitabine

-OR-

(2) Both of the following:

(a) Diagnosis of stage IV (M1) breast cancer

-AND-

(b) **One** of the following:

(i) **Both** of the following:
- HR-positive, HER2-negative disease
- Patient has already received CDK4/6 inhibitor therapy

-OR-

(ii) Triple negative disease

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Nerlynx** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Nerlynx therapy

Authorization will be issued for 12 months.

D. Breast Cancer with Brain Metastases

1. **Initial Authorization**

a. **Nerlynx** will be approved based on **all** of the following criteria:

(1) Diagnosis of breast cancer

-AND-

(2) Patient has brain metastases

-AND-

(3) Disease is HER2-positive

-AND-

(4) Used in combination with **one** of the following:

(a) capecitabine
(b) paclitaxel

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Nerlynx** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Nerlynx therapy

Authorization will be issued for 12 months.

E. Cervical Cancer

1. **Initial Authorization**

a. **Nerlynx** will be approved based on **all** of the following criteria:

(1) Diagnosis of recurrent or metastatic cervical cancer

-AND-

(2) Disease is HER2-positive

-AND-

(3) Used as second-line or subsequent therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Nerlynx** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Nerlynx therapy

Authorization will be issued for 12 months.

F. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Nerlynx [package insert]. Los Angeles, CA: Puma Biotechnology, Inc.; March 2022.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at https://www.nccn.org. Accessed June 3, 2025.

Program	Prior Authorization/Notification – Nerlynx (neratinib)
Change Control	
9/2017	New program.
9/2018	Updated background and criteria to include NCCN recommended use in patients with HER-2 positive breast cancer with recurrent brain metastases.
9/2019	Annual review with no changes to clinical coverage criteria. Updated references. Added general NCCN recommended review criteria.
4/2020	Updated background and criteria to include new indication.
5/2021	Annual review with no changes to coverage criteria. Updated references.
5/2022	Annual review with no changes to coverage criteria. Updated references.
5/2023	Annual review. Updated background. Updated criteria for metastatic breast cancer per NCCN guidelines. Updated references. Added state mandate and oncology medications footnote.
7/2023	Updated background. Added criteria for node-positive extended adjuvant therapy per NCCN guidelines. Removed oncology medications footnote. Updated reference.
7/2024	Annual review. Formatting changes to criteria without change to

	clinical intent. Updated background and references.
7/2025	Annual review. Added criteria for cervical cancer per NCCN Compendium. Updated background and references.