Clinical Policy Title:	neratinib
Policy Number:	RxA.245
Drug(s) Applied:	Nerlynx®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Neratinib (Nerlynx®) is a kinase inhibitor 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
neratinib (Nerlynx®)	Breast cancer	240 mg orally once daily (As single agent) 240mg once daily on days 1 to 21 of a 21-day cycle (in combination with capecitabine)	240 mg/day

Dosage Forms

- Tablet: 40 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Breast Cancer (must meet all):

1. Diagnosis of HER2 positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or more;
4. Prescribed in one of the following ways (a or b):
   a. In combination with capecitabine for advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in metastatic setting;

b. Given as extended adjuvant treatment of early stage HER2-overexpressed/amplified breast cancer used following 1 year of adjuvant trastuzumab based therapy;

5. 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: 12 months
Medicaid: 12 months

B. Central Nervous System Cancers (off label use) (must meet all):
1. Diagnosis of limited or extensive brain metastases in patients with HER2 positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or more;
4. 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;
5. 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: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Breast Cancer (member meets all):
1. Member is currently receiving medication that has been authorized by RxAdvance 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: 12 months
Medicaid: 12 months

B. Central Nervous System Cancers (off label use) (member meets all):
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER: human epidermal growth factor receptor
NCCN: National Comprehensive Cancer Network
HER2: Human epidermal growth receptor 2

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Herceptin® (trastuzumab) Ogivri® (trastuzumab- dkst) Ontruzant® (Trastuzumab- dttb) Herzuma® (Trastuzumab- pkrb) Trazimera™ (Trastuzumab- qyyp) Kanjinti™ (Trastuzumab-anns)	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 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	8 mg/kg

	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

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.

References

1. Nerlynx® Prescribing Information. Los Angeles, CA: Puma Biotechnology, Inc.; February 2021. Available at: https://nerlynx.com/. Accessed March 05, 2021.
2. National Comprehensive Cancer Network. Breast Cancer (Version3.2021)- Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed April 23, 2021..
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed March 05, 2021.
4. National Comprehensive Cancer Network. Central Nervous System Cancers (Version 5~~3~~.2020)- April 15, 2021, 2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf Accessed March 05, 2021.
5. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed March 05, 2021.
6. Neratinib, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at:

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy description table updated 2. Background information, indication was updated per latest prescribing information 3. Initial therapy criteria I.A.4a. was updated and I.A.4b was added per latest prescribing information 4. Continuation therapy criteria II.A.1. was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance"Appendix A was updated to include "HER2" 5. Appendix C, contraindications/boxed warnings was rephrased to "none" 6. References were updated	07/13/2020	09/14/2020
Policy was reviewed: 1. Initial and continued therapy approval criteria was created for Central Nervous System Cancers (off label use). 2. Approval duration for Initial Approval Criteria was updated to 12 months from 6 months. 3. Appendix B fixed header verbiage was updated as 'Below are suggested therapeutic alternatives..' 4. References were updated.	03/05/2020	06/10/2021