Clinical Policy: Neratinib (Nerlynx)
Reference Number: CP.PHAR.365
Effective Date: 09.05.17
Last Review Date: 11.18
Line of Business: Commercial, Medicaid

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
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 Centene Corporation® that Nerlynx is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Breast Cancer (member meets 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: 6 months

B. Other diagnoses/indications
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.
II. Continued Therapy
   A. Breast Cancer (member meets all):
      1. Currently receiving medication via Centene benefit, 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: 12 months
   
   B. Other diagnoses/indications (member meets 1 or 2):
      1. Currently receiving medication via Centene benefit and documentation supports
         positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
      2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT
         specifically listed under section III (Diagnoses/Indications for which coverage is
         NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 policies –
      CP.CPA.09 for commercial and CP.PMN.53 for Medicaid 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 for all relevant lines of business
   and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herceptin® (trastuzumab)</td>
<td>• 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</td>
<td>See regimen</td>
</tr>
</tbody>
</table>
Clinic Policy

Neratinib

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Initial dose of 8 mg/kg IV, then 6 mg/kg IV every 3 weeks for 52 weeks</td>
<td></td>
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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 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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>240 mg PO QD</td>
<td>240 mg/day</td>
</tr>
</tbody>
</table>

VI. Product Availability
Tablet: 40 mg

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>09.05.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Combined Commercial and Medicaid policies.</td>
<td>02.12.18</td>
<td></td>
</tr>
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</table>
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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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