

**Clinical Policy: Pertuzumab (Perjeta)**

Reference Number: CP.PHAR.227

Effective Date: 06.01.16

Last Review Date: 05.20

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Pertuzumab (Perjeta<sup>®</sup>) is a human epidermal growth factor receptor 2 protein (HER2)/neu receptor antagonist.

**FDA Approved Indication(s)**

Perjeta is indicated for:

- Use in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.
- Use in combination with trastuzumab and chemotherapy as:
  - Neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer;
  - Adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.

**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<sup>®</sup> that Perjeta is **medically necessary** when the following criteria are met:

**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  $\geq$  18 years;
4. Prescribed as combination therapy (*see Appendix B*);
5. Request meets one of the following (a, b or c):\*
  - a. Initial dose: 840 mg, followed by maintenance dose: 420 mg every 3 weeks;
  - 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: 6 months**

**B. Colorectal Cancer (off-label) (must meet all):**

1. Diagnosis of advanced or metastatic colorectal cancer and both of the following (a and b):
  - a. Disease is HER2 positive;
  - b. Disease is wild-type *RAS* (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use);
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. No previous use of a HER2 inhibitor therapy (e.g., trastuzumab, Kadcyra<sup>®</sup>, Tykerb<sup>®</sup>, Perjeta);
5. Prescribed in combination with trastuzumab;\*  
*\*Prior authorization may be required.*
6. Dose is within FDA maximum limit for any FDA-approved indication or 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: 6 months**

**C. 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, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Breast Cancer (must meet all):**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Perjeta for a covered indication 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 420 mg every 3 weeks;
  - 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: 12 months (total of 18 cycles if neoadjuvant or adjuvant therapy)**

**B. Other diagnoses/indications (must meet 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, HIM.PHAR.21 for health insurance marketplace, 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, HIM.PHAR.21 for health insurance marketplace, 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  
HER2: human epidermal growth factor receptor 2

KRAS: Kirsten rat sarcoma 2 viral oncogene homologue

NRAS: neuroblastoma RAS viral oncogene homologue

*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.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<p>Examples of drugs that may be used with Perjeta for breast cancer:</p> <ul style="list-style-type: none"> <li>• Chemotherapeutic agents: carboplatin, cyclophosphamide, doxorubicin</li> <li>• HER2-targeted agents: docetaxel (Taxotere<sup>®</sup>), paclitaxel, Herceptin<sup>®</sup> (trastuzumab)</li> <li>• Endocrine therapy: tamoxifen; aromatase inhibitors: anastrozole (Arimidex<sup>®</sup>), letrozole (Femara<sup>®</sup>), exemestane (Aromasin<sup>®</sup>).</li> </ul>	<p>Regimens are dependent on a variety of factors including menopausal status, treatment/progression history, clinical stage, histology, mutational and receptor status, treatment purpose (e.g., adjuvant and neoadjuvant treatment, treatment for metastatic disease).</p>	<p>Varies</p>

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): Known hypersensitivity to pertuzumab or to any of its excipients
- Boxed warning(s): Left ventricular dysfunction, embryo-fetal toxicity

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Breast cancer	<p>Initial dose of 840 mg IV, followed by maintenance dose of 420 mg IV every 3 weeks</p> <p><i>For metastatic disease, Perjeta should be administered as outlined above.</i></p>	<p>See regimens</p>

Indication	Dosing Regimen	Maximum Dose
	<p><i>For neoadjuvant treatment</i>, Perjeta should be administered for 3-6 cycles. Following surgery, patients should continue to receive Perjeta to complete 1 year of treatment (up to 18 cycles)</p> <p><i>For adjuvant treatment</i>, Perjeta should be administered for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity.</p>	

**VI. Product Availability**

Single-dose vial for injection: 420 mg/14 mL

**VII. References**

1. Perjeta Prescribing Information. South San Francisco, CA: Genentech, Inc.; December 2018. Available at [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2020/125409s124lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125409s124lbl.pdf). Accessed February 10, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at [www.nccn.org](http://www.nccn.org). Accessed February 10, 2020.
3. National Comprehensive Cancer Network Guidelines. Breast Cancer Version 2.2020. Available at [www.nccn.org](http://www.nccn.org). Accessed February 10, 2020.
4. National Comprehensive Cancer Network Guidelines. Colon Cancer Version 1.2020. Available at [www.nccn.org](http://www.nccn.org). Accessed February 10, 2020.
5. National Comprehensive Cancer Network Guidelines. Rectal Cancer Version 1.2020. Available at [www.nccn.org](http://www.nccn.org). Accessed February 10, 2020.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9306	Injection, pertuzumab, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.67.HER2 BrCa Tx and converted to new template. Requests for documentation removed. LVEF removed as a toxicity requiring discontinuation. Definition of neoadjuvant therapy added to the criteria per NCI definition. NCCN compendial recommended uses added.	05.16	06.16
Initial: Removed hypersensitivity criteria as it is not objective or measurable. Added requirement for baseline LVEF > 50% (BBW). Added examples of complete treatment regimens for early breast cancer per PI. Specified disease stage for off-label NCCN uses for	04.17	06.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
non-metastatic breast cancer. Re-auth: removed reasons to discontinue. Added requirement for documentation of positive response to therapy. Added max dosing criteria. Increased approval durations from 3/6 months to 6/12 months.		
2Q 2018 annual review: added HIM line of business; age and COC added; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; breast cancer FDA labels updated: neoadjuvant treatment with trastuzumab and docetaxel replaced with trastuzumab and chemotherapy; adjuvant treatment added; ejection fraction and number of cycles restrictions removed; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	12.19.19	05.19
Added Commercial line of business to policy.	10.08.19	
2Q 2020 annual review: added NCCN compendium-supported use of colorectal cancer; references reviewed and updated.	02.17.20	05.20

**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.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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