Clinical Policy: Pertuzumab (Perjeta)

Reference Number: LA.PHAR.227
Effective Date: 11.04.23
Last Review Date: 05.09.25~~06.10.24~~ Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description
Pertuzumab (Perjeta®) 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 (MBC) 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 Louisiana Healthcare Connections 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 ≥ 18 years;
4. Prescribed in combination with trastuzumab* and one of the following (a, b, or c):
   a. With taxane-containing chemotherapy (e.g., docetaxel or paclitaxel) for the treatment of metastatic breast cancer;
   b. With chemotherapy as neoadjuvant or adjuvant treatment (*see Appendix B*);
   c. Member was previously treated with chemotherapy and trastuzumab in absence of Perjeta;

**Prior authorization may be required*

5. Request meets one of the following (a or b):*
   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. Additional NCCN Recommended Uses (off-label) (must meet all):

1. Diagnosis of one of the following (a, b, or c):
   a. Recurrent HER2-positive salivary gland tumor;
   b. Unresectable, or resected gross residual (R2) disease, or metastatic HER2-positive gallbladder cancer or cholangiocarcinoma;
   c. Advanced or metastatic colorectal cancer and disease is all of the following (i, ii, and iii):
      i. HER2 positive;
      ii. Wild-type *RAS* (defined as wild-type in both KRAS and NRAS [i.e., KRAS and NRAS mutation-negative] as determined by an FDA-approved test for this use);
      iii. Wild-type *BRAF* (i.e., BRAF mutation-negative);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with trastuzumab;*

   **Prior authorization may be required.*
5. 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Louisiana Healthcare Connections 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 neoadjuvant or adjuvant breast cancer treatment, maximum duration does not exceed a total of 1 year treatment (up to 18 cycles);
4. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

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 policy LA.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BRAF: v-raf murine sarcoma viral oncogene homolog B1
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
KRAS: Kirsten rat sarcoma 2 viral oncogene homologue
MBC: metastatic breast cancer
NRAS: neuroblastoma RAS viral oncogene homologue

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Appendix B: Therapeutic Alternatives

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This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of drugs that may be used with Perjeta for breast cancer:	Regimens are dependent on a variety of factors including menopausal status,	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• Chemotherapeutic agents: carboplatin, cyclophosphamide, doxorubicin, docetaxel, paclitaxel • HER2-targeted agents: trastuzumab (Herceptin®, Kadcyla), lapatinib (Tykerb), Nerlynx® (neratinib) • Endocrine therapy: tamoxifen; aromatase inhibitors: anastrozole (Arimidex®), letrozole (Femara®), exemestane (Aromasin®).	treatment/progression history, clinical stage, histology, mutational and receptor status, treatment purpose (e.g., adjuvant and neoadjuvant treatment, treatment for metastatic disease).	

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

Appendix D: General Information

Residual Tumor (R) Classification:		
R0	no residual tumor	resected, negative margin
R1	microscopic residual tumor	resected, positive margin
R2	macroscopic residual tumor	resected, gross residual disease

Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	Initial dose of 840 mg IV, followed by maintenance dose of 420 mg IV every 3 weeks *For metastatic disease*, Perjeta should be administered as outlined above. *For neoadjuvant treatment*, 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) *For adjuvant treatment*, Perjeta should be administered for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity.	See regimens

V. Product Availability

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

VI. References

1. Perjeta Prescribing Information. South San Francisco, CA: Genentech, Inc.; February 2021. Available at https://www.gene.com/download/pdf/perjeta_prescribing.pdf. Accessed January ~~18, 2024~~13, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed ~~February 5, 2024~~January 27, 2025.
3. National Comprehensive Cancer Network Guidelines. Breast Cancer Version ~~1~~6.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed ~~February 5, 2024~~January 28, 2025.
4. Hermanek P and Wittekind C. Residual tumor (R) classification and prognosis. Semin Surg Oncol. 1994 Jan-Feb;10(1):12-20

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	LDH Approval Date
Converted corporate to local policy.	04.22	05.17.22
Revised criteria to clarify pertuzumab must be prescribed with trastuzumab and docetaxel or chemotherapy. Template changes applied to other diagnoses/indications. For breast cancer, added option for Perjeta without taxanes and chemotherapy for members previously treated with chemotherapy and trastuzumab without pertuzumab and revised docetaxel to taxane-containing chemotherapy per NCCN 2A recommendation; for colorectal cancer, removed requirement for no previous use of a HER2 inhibitor therapy; added unresectable or metastatic HER2-positive gallbladder cancer and cholangiocarcinoma to NCCN recommended uses (off-label); references reviewed and updated. Added verbiage this policy is for medical benefit only.	06.02.23	10.05.23
Annual review: for gallbladder cancer and cholangiocarcinoma, added option for treatment with resected gross residual (R2) disease; residual (R) tumor classification added to Appendix D; references reviewed and updated.	06.10.24	09.04.24

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
Annual review: for continued therapy, added criterion for maximum duration for neoadjuvant or adjuvant breast cancer treatment, does not exceed a total of 1 year treatment (up to 18 cycles) per PI; updated standard approval language for commercial line of business to continued therapy of "6 months or to the member's renewal date, whichever is longer;" references reviewed and updated.	05.09.25	

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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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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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