Clinical Policy: Pertuzumab (Perjeta)

Reference Number: PA.CP.PHAR.227
Effective Date: 01/2018
Last Review Date: 04/2025

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
It is the policy of PA Health & Wellness ® 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 trastuzumab only;
   b. With taxane-containing chemotherapy (e.g. docetaxel or paclitaxel);
   c. Chemotherapy as neoadjuvant or adjuvant treatment (*see Appendix B*);
   **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*).

Approval duration: 6 months

B. Additional NCCN Recommended Uses (off-label) (must meet all):

1. Diagnosis of one of the following (a, b, c or d):
   a. Recurrent HER2-positive salivary gland tumor;
   b. Unresectable or resected gross residual (R2) disease, or metastatic HER2-positive gallbladder cancer or cholangiocarcinoma;
   c. 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);

d. Meets conditions of other NCCN category 1, 2A, or 2B recommendation;

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*).

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.01) applies;
2. Documentation of positive response 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*).

Approval duration: 12 months
(Up to 18 total cycles if neoadjuvant or adjuvant therapy)

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies;

   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. 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

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 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: • Chemotherapeutic agents: carboplatin, cyclophosphamide, doxocrubicin, docetaxel, paclitaxel • HER2-targeted agents: trastuzumab (Herceptin®, Kadcyla), lapatinib (Tykerb), Nerlynx® (neratinib) • Endocrine therapy: tamoxifen; aromatase inhibitors: anastrozole (Arimidex®), letrozole (Femara®), exemestane (Aromasin®).	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).	Varies

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

IV. 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)	See regimens

Indication	Dosing Regimen	Maximum Dose
	For adjuvant treatment, Perjeta should be administered for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity.	

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 13, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 27, 2025.
3. National Comprehensive Cancer Network Guidelines. Breast Cancer Version 6.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed 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
2Q 2018 annual review: summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; references reviewed and updated.	04/2018
2Q 2019 annual review: added appendices/dosage and administration information/product availability; references reviewed and updated.	04/2019
2Q 2020 annual review: added NCCN compendium-supported use of colorectal cancer; references reviewed and updated.	04/2020
2Q 2021 annual review: added requirement for BRAF wild-type disease for off-label indication of colorectal cancer per NCCN; added NCCN compendium-supported indication of salivary gland tumors and combined with colorectal cancer criteria; references reviewed and updated.	04/2021
2Q 2022 annual review: references reviewed and updated.	04/2022

Reviews, Revisions, and Approvals	Date
Revised criteria to clarify pertuzumab must be prescribed with trastuzumab and docetaxel or chemotherapy per request from PA Ops. For colorectal cancer, removed requirement for no previous use of a HER2 inhibitor therapy.	01/2023
2Q 2023 annual review: for breast cancer, revised docetaxel to taxane-containing chemotherapy per NCCN 2A recommendation; added unresectable or metastatic HER2-positive gallbladder cancer and cholangiocarcinoma to NCCN recommended uses (off-label); references reviewed and updated.	04/2023
2Q 2024 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.	04/2024
2Q 2025 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.	04/2025