Medical Policy:

Perjeta™ (pertuzumab) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.99	March 3, 2025	

Length of Authorization

Coverage is provided for 6 months and may be renewed

Use in the neo-adjuvant and adjuvant setting is limited to up to a year of treatment (18 cycles).

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

Loading Dose

- 840 billable units x 1 dose

Maintenance Dose

- 420 billable units every 21 days

Guideline

I. Initial Approval Criteria

Coverage is provided in the following conditions:

1. Patient is 18 years or older; **AND**

2. Baseline Left ventricular ejection fraction (LVEF) within normal limits; **AND**
3. Patient has human epidermal growth factor receptor 2 (HER2)-positive***** disease; **AND**

Breast cancer †

A. Used as neoadjuvant or preoperative therapy; **AND**
   i. Patient has locally advanced, node positive, or inflammatory disease; **AND**
   ii. Used in combination with trastuzumab and chemotherapy; **OR**

B. Used as adjuvant therapy; **AND**
   i. Patient has locally advanced, node positive, or inflammatory disease; **AND**
      a. Used in combination with trastuzumab and chemotherapy; **OR**
      b. Used in combination with trastuzumab; **OR**

C. Used for recurrent unresectable or metastatic disease **OR** inflammatory breast cancer with no response to preoperative systemic therapy; **AND**
   i. Used as first-line therapy in combination with trastuzumab AND either paclitaxel or docetaxel; **OR**
   ii. Used as subsequent therapy in combination with trastuzumab with or without cytotoxic therapy ‡; **AND**
      a. Patient was previously treated with trastuzumab and chemotherapy; **AND**
      b. Patient has not previously received pertuzumab

*****HER2-positive overexpression criteria:
• Immunohistochemistry (IHC) assay 3+ ; **OR** • Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number ≥ 4.0 signals/cell; OR • Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following: o HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; OR o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; OR o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+

† FDA Approved Indication(s); **‡** Compendia recommended indication(s)

II. Renewal Criteria

Coverage can be renewed based upon the following criteria:

1. Patient continues to meet the criteria identified above; **AND**
2. Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**
3. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: cardiotoxicity (i.e. left ventricular dysfunction, cardiomyopathy); infusion-related and hypersensitivity reactions; etc.; **AND**
4. Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows:
   o Neoadjuvant and adjuvant treatment of breast cancer: LVEF is ≥ 50% OR LVEF has had an absolute decrease of < 10% from baseline
   o All other indications: LVEF is > 45% OR LVEF is 40% to 45% and absolute decrease is < 10% from baseline
5. **Use for adjuvant OR neo-adjuvant Breast Cancer treatment** is limited to up to a year of treatment (total of 18 cycles).

Limitations/Exclusions

Perjeta is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

Code	Description
J9306	Injection, pertuzumab, 1 mg; 1 mg = 1 billable unit

Applicable NDCs

Code	Description
50242-0145-xx	Perjeta 420 mg/14 mL solution for injection

ICD-10 Diagnoses

Code	Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola , unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast

C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
Z85.3	Personal history of malignant neoplasm of breast

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	03/03/2025	Annual Review: Initial Criteria: Breast cancer † Removed the following to reword and add back: “Used as adjuvant treatment; AND Patient has locally advanced disease or early stage disease at high risk of recurrence; AND Used in combination with a trastuzumab-based regimen; OR Used as neoadjuvant treatment for breast preservation; AND Patient has locally advanced, inflammatory or early stage disease; AND Used in combination with a trastuzumab-based regimen; OR Used for recurrent or metastatic disease; AND Used as first line therapy in combination with trastuzumab and paclitaxel or docetaxel; OR Used as second-line therapy in combination with trastuzumab ‡: AND Previously treated with trastuzumab-based therapy; AND Patient has not previously received pertuzumab” added back as: “Used as neoadjuvant or preoperative therapy; AND Patient has locally advanced, node positive, or inflammatory disease; AND Used in combination with trastuzumab and chemotherapy; OR Used as adjuvant therapy; AND Patient has locally advanced, node positive, or inflammatory disease; AND Used in combination with trastuzumab and chemotherapy; OR Used in combination with trastuzumab; OR Used for recurrent unresectable or metastatic disease OR inflammatory breast cancer with no response to preoperative systemic therapy; AND Used as first-line therapy in combination with trastuzumab AND either

		paclitaxel or docetaxel; OR Used as subsequent therapy in combination with trastuzumab with or without cytotoxic therapy ‡; ANDPatient was previously treated with trastuzumab and chemotherapy; AND Patient has not previously received pertuzumab Renewal criteria: removed: "Left ventricular ejection fraction (LVEF) is >45% OR LVEF is ≥40% and absolute decrease is <10% from baseline (results must be less than 3 months old); AND" replaced with: "Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows: o Neoadjuvant and adjuvant treatment of breast cancer: LVEF is ≥ 50% OR LVEF has had an absolute decrease of < 10% from baseline o All other indications: LVEF is > 45% OR LVEF is 40% to 45% and absolute decrease is < 10% from baseline"
EmblemHealth & ConnectiCare	1/18/2024	Annual Review: updated HER 2 overexpression criteria
EmblemHealth & ConnectiCare	5/22/2023	Annual Review: no criteria changed
EmblemHealth & ConnectiCare	09/20/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	01/01/2020	Annual review

References

1. Perjeta [package insert]. South San Francisco, CA; Genentech, Inc.; December 2018. Accessed December 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pertuzumab. National Comprehensive Cancer Network, 2018. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2018.
3. Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012;366(2):109-119.
4. Gianni L, Pienkowski T, Im YH, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomized multicentre, open-label, phase 2 trial. Lancet Oncol. 2012 Jan;13(1):25-32.
5. Baselga J, Cortes J, Kim SB, et al. CLEOPATRA Study Group. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med*. 2012;366:109-119.
6. Schneeweiss A., Chia S., Hickish T., et al; Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). *Ann Oncol* 2013; 24 (9): 2278-2284.
7. Von MG, Baselga J, Bradbury I, et al. Adjuvant Pertuzumab and Herceptin in initial therapy of Breast Cancer: APHINITY (BIG4-11/BO25126/TOC4939g) [abstract]; Cancer Res 2011; 71 (Suppl 24); Abstract OT1-02-04.