

Perjeta[®] (pertuzumab) (Intravenous)

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I. Length of Authorization

Coverage is provided for 6 months and may be renewed

- Use for neo-adjuvant and adjuvant breast cancer is limited to a total of 1 year of treatment [18 cycles] (**Note: When used for metastatic breast cancer, therapy may be continued until disease progression or unmanageable toxicity.*)

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Perjeta 420 mg/14mL solution for injection:

- **Loading Dose:** 2 vials
- **Maintenance Doses:** 1 vial every 21 days

B. Max Units (per dose and over time) [HCPCS Unit]:

Loading Dose

- 840 billable units x 1 dose

Maintenance Dose

- 420 billable units every 21 days

III. Initial Approval Criteria¹

Coverage is provided in the following conditions:

- Patient is 18 years or older; **AND**

Universal Criteria

- Left ventricular ejection fraction (LVEF) within normal limits prior to initiating therapy and will be assessed at regular intervals during treatment; **AND**
- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease; **AND**

Breast Cancer † 1,2,5,6,7,8,9

- 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**
 - Patient has hormone receptor negative or positive disease; **AND**
 - Used as first-line therapy in combination with trastuzumab and either paclitaxel OR docetaxel; **OR**
 - Used as second-line therapy in combination with a trastuzumab-based regimen ‡; **AND**
 - Patient was previously treated with trastuzumab-based therapy; **AND**
 - Patient has not previously received pertuzumab

Colorectal Cancer ‡^{2,10}

- Used for RAS and BRAF wild-type (WT) disease in combination with trastuzumab in patients who have not previously received HER2-targeted therapy; **AND**
 - Used as subsequent therapy for progression of advanced or metastatic disease; **AND**
 - Patient must have been previously treated with oxaliplatin-based therapy without irinotecan, irinotecan-based therapy without oxaliplatin, oxaliplatin and irinotecan, or fluoropyrimidine-based therapy without irinotecan or oxaliplatin; **OR**
 - Used as primary therapy, treatment of disease that remains unresectable after primary therapy, or treatment following local therapy; **AND**
 - Patient has locally unresectable (or medically inoperable) or metastatic disease; **AND**
 - Patient is not appropriate for intensive therapy; **OR**
- Used as adjuvant therapy for RAS and BRAF wild-type (WT) disease in combination with trastuzumab in patients who are not candidates for intensive therapy; **AND**
 - Patient converted from unresectable to resectable disease after primary therapy; **OR**
 - Patient has previously received chemotherapy

*HER2-positive overexpression criteria:^{3,4}

- 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:
 - HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; **OR**
 - HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; **OR**
 - 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)

IV. Renewal Criteria¹

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: cardiotoxicity (e.g., left ventricular dysfunction, cardiomyopathy, etc.), severe infusion-related and hypersensitivity reactions/anaphylaxis, etc.; **AND**
- Left ventricular ejection fraction (LVEF) is $>45\%$ OR LVEF is $\geq 40\%$ and absolute decrease is $<10\%$ from baseline; **AND**
- Use for neoadjuvant and adjuvant breast cancer treatment is limited to a total of 1 year of treatment (total of 18 cycles)

V. Dosage/Administration

Indication	Dose
Breast Cancer	840 mg intravenously x 1 dose, then 420 mg intravenously every 21 days thereafter until disease progression or unmanageable toxicity <ul style="list-style-type: none"> • Neoadjuvant therapy consists of 3 to 6 cycles prior to surgery • Use for neoadjuvant and adjuvant early breast cancer treatment is limited to a total of 1 year of treatment (total of 18 cycles) <i>*Note: When used for metastatic breast cancer, therapy may be continued until disease progression or unmanageable toxicity.</i>
Colorectal Cancer	840 mg intravenously x 1 dose, then 420 mg intravenously every 21 days thereafter until disease progression or unmanageable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

J9306 - Injection, pertuzumab, 1 mg; 1 mg = 1 billable unit

NDC(s):

VII. References

1. Perjeta [package insert]. South San Francisco, CA; Genentech, Inc.; January 2020. Accessed April 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pertuzumab. National Comprehensive Cancer Network, 2020. 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 April 2020.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 4.2020. National Comprehensive Cancer Network, 2020. 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 Guidelines, go online to NCCN.org. Accessed April 2020.
4. Wolff AC, Hammond EH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *J Clin Oncol* 2018;36:2105-2122.
5. 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.
6. 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 randomised multicentre, open-label, phase 2 trial. *Lancet Oncol.* 2012 Jan;13(1):25-32.
7. 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.
8. 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.
9. 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.
10. Hainsworth JD, Meric-Bernstam F, Swanton C, et al. Targeted Therapy for Advanced Solid Tumors on the Basis of Molecular Profiles: Results From MyPathway, an Open-Label, Phase IIa Multiple Basket Study. *Clin Oncol.* 2018 Feb 20;36(6):536-542.
11. CGS Administrators, LLC. Local Coverage Article for Billing and Coding: Pertuzumab - J9306 (A57264). Centers for Medicare & Medicaid Services, Inc. Updated on 09/18/2019 with effective date of 09/26/2019. Accessed April 2020.

12. Palmetto GBA, LLC. Local Coverage Article: Billing and Coding: Chemotherapy (A56141). Centers for Medicare and Medicaid Services, Inc. Updated on 03/24/2020 with effective date 04/30/2020. Accessed April 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
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

ICD-10	ICD-10 Description
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

ICD-10	ICD-10 Description
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
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.3	Personal history of malignant neoplasm of breast

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): 15	NCD/LCD/LCA Document (s): A57264
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=A57264&bc=gAAAAAAAAAAAA&	

Jurisdiction(s): J & M	NCD/LCD/LCA Document (s): A56141
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAAA&	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC