Phesgo™ (pertuzumab, trastuzumab and hyaluronidase-zzxf) (Subcutaneous)

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I. Length of Authorization

Coverage is provided for six months and may be renewed.

- Use in the neoadjuvant/adjuvant setting is limited to a total of 1 year (up to 18 cycles)

II. Dosing Limits

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

- Phesgo 1200 mg (P)/600 mg (T)/30,000 units (hyu) single-dose vial: 1 vial as initial dose
- Phesgo 600 mg (P)/600 mg (T)/20,000 units (hyu) single-dose vial: 1 vial every 21 days

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

Breast Cancer

- Loading dose: 1200 mg (P)/600 mg (T)/30,000 units (hyu) for 1 dose
- Maintenance dose: 600 mg (P)/600 mg (T)/20,000 units (hyu) every 21 days

III. Initial Approval Criteria [1,2,3,4,5]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease; **AND**
- Therapy will not be used in combination with pertuzumab, trastuzumab (or trastuzumab biosimilar product [e.g., Ogivri, Kanjinti, Trazimera, Herzuma, Ontruzant]), or trastuzumab and hyaluronidase-oysk (Herceptin Hylecta); **AND**
- Therapy will not be substituted for or with pertuzumab or any trastuzumab-based formulation (i.e., trastuzumab [or trastuzumab biosimilar product], ado-trastuzumab emtansine, fam-trastuzumab deruxtecan-nxki, trastuzumab-hyaluronidase, etc.); **AND**
- Patient does not have a known hypersensitivity to an alternative formulation of trastuzumab or pertuzumab; **AND**

Breast Cancer †

- Used as neoadjuvant therapy; **AND**
  - Patient has locally advanced, inflammatory, or early stage disease; **OR**
- Used as adjuvant therapy; **AND**
  - Patient has locally advanced or node positive disease OR early stage disease at high risk of recurrence; **OR**
- Used for recurrent or metastatic disease; **AND**
  - Used as first-line therapy in combination with either paclitaxel or docetaxel; **OR**
  - Used as second-line therapy ‡; **AND**
    - Patient was previously treated with trastuzumab and chemotherapy; **AND**
    - Patient has not previously received pertuzumab

† FDA Approved Indication(s); ‡ Compendia recommended Indication(s); Φ Orphan Drug

***HER2-positive overexpression criteria:**[6,7]

- 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+

IV. Renewal Criteria [1]

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 the following: cardiotoxicity (e.g., left ventricular dysfunction, cardiomyopathy, etc.), pulmonary toxicity (i.e., pneumonitis), neutropenia, infusion-related reactions, etc.; **AND**

  Breast Cancer (neoadjuvant or adjuvant treatment)
  - Left ventricular ejection fraction (LVEF) is ≥ 50% OR LVEF absolute decrease is < 10% from pre-treatment baseline (LVEF results must be within the previous 3 months); **AND**
  - Patient has not exceeded a maximum of 1 year of therapy (18 cycles)

Breast Cancer (metastatic)

- Left ventricular ejection fraction (LVEF) is > 45% OR is between 40-45% and absolute decrease is < 10% from pre-treatment baseline (LVEF results must be within the previous 3 months)

V. Dosage/Administration

Indication	Dose
Breast Cancer	**Initial** Administer 1200 mg (P)/600 mg (T)/30,000 units (hyl) subcutaneously. **Maintenance** Administer 600 mg (P)/600 mg (T)/20,000 units (hyl) subcutaneously every 3 weeks ○ Neo-adjuvant therapy is administered as 3-6 cycles initially, then continued following surgery to complete 1 year of treatment (up to 18 cycles) ○ Adjuvant therapy is administered for a total of 1 year (up to 18 cycles) or until disease recurrence or unacceptable toxicity ○ Metastatic or recurrent breast cancer should be treated until disease progression or until unacceptable toxicity.
Note: – *To be administered by a health care professional as a subcutaneous use only in the thigh. Do not administer intravenously.* – *Do not substitute for or with ado-trastuzumab emtansine or fam-trastuzumab deruxtecan-nxki.* – *Phesgo has different dosage and administration instructions than intravenous pertuzumab, intravenous trastuzumab, and subcutaneous trastuzumab when administered alone.* – *Refer to the package insert for timing and sequence of dosing with other chemotherapy.* – *Refer to the package insert for transitioning from trastuzumab and/or pertuzumab intravenous.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J9999 – Not otherwise classified, antineoplastic drugs
- C9399 – Unclassified drugs or biologicals *(hospital outpatient use)*

NDC:

- Phesgo 1200 mg/600 mg/30,000 units (providing 1200 mg pertuzumab, 600 mg trastuzumab and 30,000 units hyaluronidase per 15 mL) single-dose vials: 50242-0245-xx
- Phesgo 600 mg/600 mg/20,000 units (providing 600 mg pertuzumab, 600 mg trastuzumab and 20,000 units hyaluronidase per 10 mL) single-dose vials: 50242-0260-xx

VII. References

1. Phesgo [package insert]. South San Francisco, CA; Genentech, Inc; June 2020. Accessed August 2020.

2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pertuzumab, trastuzumab and hyaluronidase human. 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 August 2020.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 5.2020. 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 August 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. Tan AR, Im SA, Mattar A, et al. Subcutaneous administration of the fixed-dose combination of trastuzumab and pertuzumab in combination with chemotherapy in HER2-positive early breast cancer: Primary analysis of the phase III, multicenter, randomized, open-label, two-arm FeDeriCa study [Abstract]. In: Proceedings of the 2019 San Antonio Breast Cancer Symposium; 2019 Dec 10-14; San Antonio, TX. Philadelphia (PA): AACR; Cancer Res 2020;80(4 Suppl):Abstract nr PD4-07.
6. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 5/21/20 . Identifier NCT03674112, A Study to Evaluate Patient Preference and Satisfaction of Subcutaneous Administration of the Fixed-Dose Combination of Pertuzumab and Trastuzumab in Participants With HER2-Positive Early Breast Cancer (PHranceSCa); [Accessed 7/2/20]; Available from: https://clinicaltrials.gov/ct2/show/NCT03674112?term=NCT03674112&draw=2&rank=1.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 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 female breast
C50.022	Malignant neoplasm of nipple and areola, left female breast
C50.029	Malignant neoplasm of nipple and areola, unspecified female 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

ICD-10	ICD-10 Description
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

ICD-10	ICD-10 Description
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

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), and 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): N/A

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.
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