MEDICAL MUTUAL®

Drug Policy

Policy:	**20200802**	**Initial Effective Date: 9/18/2020**
Code(s):	**HCPCS J9316**	**Annual Review Date: 03/19/2024**
SUBJECT:	**Phesgo™ (pertuzumab, trastuzumab and hyaluronidase-zzxf)**	**Last Revised Date: 03/19/2024**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

POLICY STATEMENT

This policy involves the use of Phesgo. Prior authorization is recommended for medical benefit coverage of Phesgo. Approval is recommended for those who meet the conditions of coverage in the **Initial Approval and Renewal Criteria, Preferred Drug (when applicable), Dosing/Administration, Length of Authorization, and Site of Care (when applicable)** for the diagnosis provided. The requirement that the patient meet the Criteria and Preferred Drug for coverage of the requested medication applies to the initial authorization only. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

I. Length of Authorization [1]

Coverage is provided for 6 months and may be renewed (unless otherwise specified).

- Neoadjuvant and adjuvant therapy may be authorized for a total of 1 year (up to 18 cycles).

II. Dosing Limits

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

- Phesgo (1,200 mg pertuzumab/600 mg trastuzumab/30,000 units hyaluronidase) single-dose vial: 1 vial as initial dose
- Phesgo (600 mg pertuzumab/600 mg trastuzumab/20,000 units hyaluronidase) single-dose vial: 1 vial every 21 days

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

- Initial Dose: 180 billable units x 1 dose
- Maintenance Dose: 120 billable units every 21 days

III. Initial Approval Criteria [1-5]

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 as determined by an FDA-approved or CLIA-compliant test❖; **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-oysk, etc.); **AND**

Breast Cancer † ‡ [1-7]

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

❖ *If confirmed using an immunotherapy assay-http://www.fda.gov/companiondiagnostics*

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

***HER2-positive overexpression criteria: [6,8]**

- 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 may be renewed based upon the following criteria:

- Patient continues to meet the 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., hypertension, arrhythmias, left ventricular dysfunction, cardiac failure, cardiomyopathy), pulmonary toxicity (e.g., angioedema, interstitial pneumonitis, acute respiratory distress syndrome, etc.), neutropenia/febrile neutropenia, severe administration-related reactions (e.g., hypersensitivity reactions, anaphylaxis), etc.; **AND**
- Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows:
  - Neoadjuvant and adjuvant treatment of breast cancer: LVEF is ≥ 50% OR LVEF has had an absolute decrease of < 10% from pre-treatment baseline; **OR**
  - All other indications: LVEF is > 45% OR LVEF is 40% to 45% and absolute decrease is < 10% from pre-treatment baseline

Breast Cancer (neoadjuvant or adjuvant treatment)

- Patient has not exceeded a maximum of 1 year of therapy (total of 18 cycles)

V. Dosage/Administration [1]

Indication	Dose
Breast Cancer	**Initial Dose** Administer 1,200 mg pertuzumab/600 mg trastuzumab/30,000 units hyaluronidase subcutaneously **Maintenance Dose** Administer 600 mg pertuzumab/600 mg trastuzumab/20,000 units hyaluronidase subcutaneously every 3 weeks • Neoadjuvant therapy: administer for 3-6 cycles as part of a chemotherapy containing regimen, then continue following surgery to complete 1 year of treatment (up to 18 cycles) or until disease recurrence or unacceptable toxicity • Adjuvant therapy: administer for a total of 1 year (up to 18 cycles) or until disease recurrence or unacceptable toxicity • Recurrent or metastatic breast cancer: administer until disease progression or until unacceptable toxicity
***Note**:* – *To be administered by a health care professional for subcutaneous use only in the thigh. Do not administer intravenously.* – *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:

- J9316 – Injection, pertuzumab, trastuzumab, and hyaluronidase-zzxf, per 10 mg; 1 billable unit = 10 mg

NDC(s):

- Phesgo (1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase per 15 mL) single-dose vial: 50242-0245-xx
- Phesgo (600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase per 10 mL) single-dose vial: 50242-0260-xx

VII. References

1. Phesgo [package insert]. South San Francisco, CA; Genentech, Inc; June 2020. Accessed January 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pertuzumab, trastuzumab and hyaluronidase-zzxf. National Comprehensive Cancer Network, 2024. 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 2024.

3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 1.2024. National Comprehensive Cancer Network, 2024. 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 January 2024.
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.
7. Gennari A, André F, Barrios CH, et al.; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer. Ann Oncol. 2021 Dec;32(12):1475-1495. doi: 10.1016/j.annonc.2021.09.019. Epub 2021 Oct 19. PMID: 34678411.
8. Wolff AC, Hammond MEH, 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 Jul 10;36(20):2105-2122. doi: 10.1200/JCO.2018.77.8738. Epub 2018 May 30. PMID: 29846122.
9. First Coast Service Options, Inc. Local Coverage Article: Billing and Coding: Trastuzumab – Trastuzumab Biologics (A56660). Centers for Medicare & Medicaid Services, Inc. Updated on 10/08/2021 with effective date 10/01/2021. Accessed January 2024.

MEDICAL MUTUAL®

Drug Policy

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J9316

Edits and Denials:

Prior approval: Prior approval is required for Phesgo **(HCPCS Codes J9316)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Codes J9316** will pend with **Remark Code M3M or M4M** and will be adjudicated in accordance with the Corporate Medical Policy.

Liability: A participating provider will be required to write off charges denied as not medically necessary.