MEDICAL MUTUAL®

Drug Policy

Policy:	**20200802**	**Initial Effective Date: 9/18/2020**
Code(s):	**HCPCS J9316**	**Annual Review Date: 06/19/2025**
SUBJECT:	**Phesgo™ (pertuzumab, trastuzumab and hyaluronidase-zzxf)**	**Last Revised Date: 06/19/2025**

Subject to: ☐Site of Care
☒Medication

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

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**

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

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 or any trastuzumab-based formulation; **AND**
- Therapy will not be substituted for or with pertuzumab or any trastuzumab-based formulation; **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, pT2-3 and pN0, inflammatory, or node positive disease OR early stage disease at high risk of recurrence; **OR**
  - Used after completion of planned chemotherapy and following mastectomy or breast-conserving surgery; **AND**
    - Patient has ≥ ypT0N0 or pCR disease by axillary staging; **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 with or without cytotoxic 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**

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

- 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**
- Duration of authorization has not been exceeded *(refer to section I);* **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

V. Dosage/Administration [1]

Indication	Dose
Breast Cancer	**Initial Dose** Administer 1,200 mg pertuzumab/600 mg trastuzumab/30,000 units hyaluronidase subcutaneously

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

	Maintenance Dose Administer 600 mg pertuzumab/600 mg trastuzumab/20,000 units hyaluronidase subcutaneously every 3 weeks • Neoadjuvant therapy: administer for 3-9 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; November 2024. Accessed April 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pertuzumab, trastuzumab and hyaluronidase-zzxf. National Comprehensive Cancer Network, 2025. 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 2025.

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 4.2025. National Comprehensive Cancer Network, 2025. 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 May 2025.
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. O'Shaughnessy J, Sousa S, Cruz J, et al. PHranceSCa study group. Preference for the fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection in patients with HER2-positive early breast cancer (PHranceSCa): A randomised, open-label phase II study. Eur J Cancer. 2021 Jul;152:223-232. doi: 10.1016/j.ejca.2021.03.047. Epub 2021 Jun 16. PMID: 34147014.
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.

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

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

ICD-10	ICD-10 Description
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
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

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

ICD-10	ICD-10 Description
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

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio

Prior approval is required for HCPCS Codes J9316

This document is subject to the disclaimer found at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx and is subject to change. Always verify with the most current version at https://www.medmutual.com/For-Providers/Policies-and-Standards/CorporateMedicalDisclaimer.aspx

© 2025 Medical Mutual of Ohio