Phesgo (pertuzumab, trastuzumab, and hyaluronidase-zzxf)
PAM – 064

Iowa Medicaid Program	Prior Authorization	**Effective Date**	01/01/2021
Revision Number	3	**Last Reviewed**	10/17/2025
Reviewed By	Medicaid Medical Director	**Next Review**	10/16/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	10/20/2023

Overview

Medication: [1]	pertuzumab, trastuzumab, and hyaluronidase-zzxf
Brand Name:	Phesgo®
Pharmacologic Category:	Antineoplastic; HER2/neu receptor antagonist (pertuzumab and trastuzumab) and endoglycosidase (hyaluronidase) combination
FDA-Approved Indication(s): 1. Early Breast Cancer (EBC) – In combination with chemotherapy for: a. Neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early-stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer. b. Adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence. 2. Metastatic Breast Cancer (MBC) – In combination with docetaxel for treatment of: a. Adult patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. ➢ Select patients for therapy based on HER2 protein overexpression or HER2 gene amplification in tumor specimens using an FDA-approved diagnostic test.	
How Supplied:	Single-dose vial containing either: • 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase per 15 mL • 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase per 10 mL
Dosage and Administration:	See Appendix A for dosage and administration information
Benefit Category:	Medical

BOXED WARNING: CARDIOMYOPATHY, EMBRYO-FETAL TOXICITY, AND PULMONARY TOXICITY

Cardiomyopathy: Phesgo® administration can result in subclinical and clinical cardiac failure. The incidence and severity were highest in patients receiving Phesgo® with anthracycline-containing regimens. Evaluate cardiac function prior to and during treatment with Phesgo®. Discontinue treatment in patients receiving adjuvant therapy and withhold in patients with metastatic disease for clinically significant decrease in left ventricular function.

Embryo-fetal toxicity: Exposure to Phesgo® can result in embryo-fetal death and birth defects, including oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception.

BOXED WARNING: CARDIOMYOPATHY, EMBRYO-FETAL TOXICITY, AND PULMONARY TOXICITY
Pulmonary toxicity: Phesgo® administration can result in serious and fatal pulmonary toxicity. Discontinue PHESGO for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. Monitor patients until symptoms completely resolve.

Descriptive Narrative

Globally, breast cancer is the most frequently diagnosed malignancy, accounting for over two million cases each year. It is also the leading cause of cancer death in women worldwide. In the United States, breast cancer is the most common female cancer, and the second most common cause of cancer death in women.[2] An estimated 3,010 new cases of breast cancer in females will be diagnosed in Iowa in 2024, making it the second most commonly diagnosed cancer in the state (second only to prostate cancer), and with an estimated 370 deaths, it is the fourth highest cause of cancer deaths in Iowa in 2024.[3]

Breast cancer is a heterogenous, phenotypically diverse disease composed of several biologic subtypes that have distinct behavior. Amplification or over-expression of the human epidermal growth factor receptor 2 *(HER2)* oncogene* is present in approximately 15 percent of primary invasive breast cancers. Women with both early-stage and metastatic breast cancer** that meet criteria for HER2 positivity are treated with regimens including HER2-directed therapy.[4]

Phesgo® is a combination of pertuzumab and trastuzumab, HER2/neu receptor antagonists, and hyaluronidase, an endoglycosidase.

- Pertuzumab targets the extracellular dimerization domain (subdomain II) of HER2 and inhibits ligand-initiated intracellular signaling through two major signaling pathways, which can result in cell growth arrest and apoptosis, respectively.
- Trastuzumab binds to subdomain IV of the extracellular domain of the HER2 protein to inhibit the ligand-independent, HER2 mediated cell proliferation and PI3K signaling pathway in human tumor cells that overexpress HER2.
- While pertuzumab alone inhibited the proliferation of human tumor cells, the combination with trastuzumab augmented anti-tumor activity in HER2-overexpressing xenograft models.
- Hyaluronan is a polysaccharide found in the extracellular matrix of the subcutaneous tissue. It is depolymerized by the enzyme hyaluronidase. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. The effects of hyaluronidase are reversible and permeability of the subcutaneous tissue is restored within 24 to 48 hours.[5]

* Human epidermal growth factor receptor 2 *(HER2)* is a growth-promoting protein on the outside of all breast cells. Breast cancer cells with higher-than-normal levels of HER2 are referred to as HER2-positive.

** Metastatic breast cancer (MBC). Also called Stage IV, MBC is breast cancer that has spread to another part of the body, commonly the liver, brain, bones, or lungs.

Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.[6,7]

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):[8]

- Breast Cancer (v.4.2024 – July 3, 2024)

NCCN Guidelines® Recommendation(s) – Breast Cancer
(1) Preoperative/adjuvant therapy, HER2-positive [a] a. Preferred Regimens i. TCHP (docetaxel/carboplatin/trastuzumab/pertuzumab): Category 2A [b] b. Useful in Certain Circumstances i. Doxorubicin/cyclophosphamide followed by paclitaxel + trastuzumab + pertuzumab: Category 2A [b, c, d] ii. Paclitaxel + trastuzumab + pertuzumab: Category 2A [b, d] c. Other Recommended Regimens i. Doxorubicin/cyclophosphamide followed by docetaxel + trastuzumab + pertuzumab: Category 2A [b, c, d] (2) Recurrent unresectable (local or regional) or Stage IV (M1) disease [e] a. HR-positive or -negative and HER2-positive, first line i. Pertuzumab + trastuzumab + docetaxel: Category 1, Preferred [b, f] ii. Pertuzumab + trastuzumab + paclitaxel: Category 2A, Preferred [b, f]
[a] Alternative taxanes (i.e., docetaxel, paclitaxel, albumin-bound paclitaxel) may be substituted for select patients due to medical necessity (i.e., hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of albumin-bound paclitaxel should not exceed 125 mg/m^2. [b] Pertuzumab, trastuzumab, and hyaluronidase-zzxf injection for subcutaneous use may be substituted anywhere that the combination of intravenous pertuzumab and intravenous trastuzumab are given as part of systemic therapy. Pertuzumab, trastuzumab, and hyaluronidase-zzxf injection for subcutaneous use has different dosing and administration instructions compared to the intravenous products. [c] It is acceptable to change the administration sequence to taxane (with or without HER2-targeted therapy) followed by doxorubicin/cyclophosphamide. [d] Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided. [e] Assess for germline *BRCA1/2* mutations in all patients with recurrent or metastatic breast cancer to identify candidates for PARP inhibitor therapy. While olaparib and talazoparib are FDA-indicated in HER2-negative disease, the panel supports use in any breast cancer subtype associated with a germline mutation. There is lower-level evidence for HER2-positive tumors, therefore category 2A for this setting. [f] Maintenance trastuzumab/pertuzumab after response (with concurrent endocrine therapy if ER+ and HER2+ metastatic breast cancer).

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Criteria

Prior authorization is required.

Phesgo® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of human epidermal growth factor receptor 2 *(HER2)*-positive (HER2+) breast cancer; **AND**
2. Member is 18 years of age or older; **AND**
3. Member meets **ONE** of the following (a, b, or c):
    a. Diagnosis of HER2+, locally advanced, inflammatory, or early-stage breast cancer (EBC) (either > 2 cm in diameter or node positive) and:
        1) Phesgo® is prescribed every 3 weeks for 3–6 cycles as part of a complete neoadjuvant treatment regimen for EBC; **AND**
        2) Following surgery, member will receive Phesgo® to complete one year of treatment (up to 18 cycles) or until disease recurrence or unmanageable toxicity; **OR**
    b. Diagnosis of HER2+ EBC at high-risk of recurrence and:
        1) Phesgo® is prescribed every 3 weeks as part of a complete adjuvant treatment regimen for EBC, including standard anthracycline- and/or taxane-based chemotherapy; **AND**
        2) Treatment plan is for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity, whichever occurs first; **OR**
    c. Diagnosis of metastatic breast cancer (MBC) and is prescribed every 3 weeks (with docetaxel) until disease progression or unacceptable toxicity, whichever occurs first; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**

5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed initial dose of 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase, followed by 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase every 3 weeks; or,
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Phesgo® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase every 3 weeks; or,
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	• Neoadjuvant therapy: 5 months total (6 cycles) • Adjuvant therapy: 12 months total (18 cycles) • MBC: until disease recurrence or unmanageable toxicity
Quantity Limits	**Initial:** 1,200 mg pertuzumab, 600 mg trastuzumab, 30,000 units hyaluronidase **Subsequent:** 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase every 3 weeks	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9316	Injection, pertuzumab, trastuzumab, and hyaluronidase-zzxf, per 10 mg

ICD-10	Description
C50.11-C50.929	Malignant neoplasm of breast [HER2 positive] [not covered if HER2 negative]
C79.81	Secondary malignant neoplasm of breast
D05.00-D05.92	Carcinoma in situ of breast

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units /Pkg
50242-0245-01 (1,200 mg, 600 mg, & 30,000 units/15 mL)	Genentech, Inc. (50242)	10 mg	1	EA	180
50242-0260-01 (600 mg, 600 mg, & 20,000 units/10 mL)	Genentech, Inc. (50242)	10 mg	1	EA	120

Appendix A: Dosing and Administration

Dosing & schedule for FDA-approved indications of Phesgo® listed below. For dosing instructions of agents administered in combination with Phesgo®, see manufacturer's prescribing information for each respective agent.

Administration

- Phesgo® should be administered subcutaneously in the thigh. Do not administer intravenously.
- Must always be administered by a healthcare professional.
- Observe patients for a minimum of 30 minutes after initial dose of Phesgo® and 15 minutes after each maintenance dose for signs or hypersensitivity symptoms or administration-related reactions. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use.
- In patients receiving an anthracycline-based regimen for early breast cancer, administer Phesgo® following completion of the anthracycline.
- In patients receiving Phesgo® for early breast cancer with docetaxel or paclitaxel, administer docetaxel or paclitaxel after Phesgo®.
- In patients receiving Phesgo® for metastatic breast cancer with docetaxel, administer docetaxel after Phesgo®.
- See complete prescribing information for dosing recommendations in patients transitioning to Phesgo® from IV pertuzumab/trastuzumab.
- See complete prescribing information for dose modification recommendations in the event of missed or delayed doses, or adverse reactions.
- See following tables for dosing and administration recommendations for Phesgo®.

Recommended Dosage and Administration Instructions

Dose	Strength (pertuzumab, trastuzumab, hyaluronidase)	Administration Instructions
Initial Dose	1,200 mg, 600 mg, and 30,000 units	Subcutaneously over approximately 8 minutes
Maintenance Dose	600 mg, 600 mg, and 20,000 units	Subcutaneously over approximately 5 minutes every 3 weeks

Recommended Dosing Schedule

Neoadjuvant Treatment of Breast Cancer

- Administer every 3 weeks for 3 to 6 cycles as part of a treatment regimen for early breast cancer.
- Refer to the prescribing info for pertuzumab, administered in combination with trastuzumab and chemotherapy, for recommended dose and dosage modifications.
- Following surgery, patients should continue to receive Phesgo® to complete 1 year of treatment (up to 18 cycles) or until disease recurrence or unmanageable toxicity, whichever occurs first, as a part of a complete regimen for early breast cancer.

Adjuvant Treatment of Breast Cancer

- Administer every 3 weeks for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity, whichever occurs first, as part of a complete regimen for early breast cancer, including standard anthracycline- and/or taxane-based chemotherapy. Start Phesgo® on Day 1 of the first taxane-containing cycle.

Treatment of Metastatic Breast Cancer

- When administered with Phesgo®, the recommended initial dose of docetaxel is 75 mg/m^2 administered as an IV infusion. The dose may be escalated to 100 mg/m^2 administered every 3 weeks if the initial dose is well tolerated.
- Administer Phesgo® until disease progression or unmanageable toxicity, whichever occurs first.

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Phesgo® prescribing information (11/2024). Genentech, Inc.: South San Francisco, CA. Available online: www.phesgo-hcp.com. Accessed August 13, 2025.

[2] Joe BN. Clinical features, diagnosis, and staging of newly diagnosed breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed July 29, 2024.

[3] American Cancer Society: Cancer Statistics Center. State of Iowa. Available online at cancerstatisticscenter.cancer.org/states/iowa. Accessed July 29, 2024.

[4] Yamauchi H, Bleiweiss IJ. HER2 and predicting response to therapy in breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed September 6, 2024.

[5] See reference for Phesgo® prescribing information above.

[6] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[7] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[8] NCCN Clinical Practice Guidelines in Oncology. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- Breast Cancer (v.4.2024 – July 3, 2024)

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

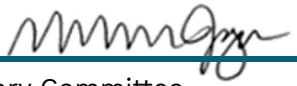
Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
10/17/2025	CAC	Annual review. No changes.	3
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/18/2024	CAC	Annual review. Reviewed NCCN Guidelines; no changes. Updated references.	2
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee