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Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Antineoplastic Agents	**Original Policy Date:**	August 7, 2020
Subject:	Phesgo	**Page:**	1 of 5

Last Review Date: March 6, 2026

Phesgo

Description

Phesgo (pertuzumab, trastuzumab, and hyaluronidase-zzxf)

Background

Phesgo is a combination of pertuzumab and trastuzumab, HER2/neu receptor antagonists, and hyaluronidase, an endoglycosidase. Pertuzumab blocks ligand-dependent heterodimerization of HER2 with other HER family members, including EGFR, HER3, and HER4. Trastuzumab inhibits HER2 mediated cell proliferation and PI3K signaling pathway in human cells that overexpress HER2. Both pertuzumab and trastuzumab-mediated antibody-dependent cell-mediated cytotoxicity have been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan (1).

Regulatory Status

FDA-approved indications: Phesgo is indicated for: (1)

1. Use in combination with chemotherapy as:
    a. Neoadjuvant treatment of 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 patients with HER2-positive early breast cancer at high risk of recurrence
2. Use in combination with docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease

Phesgo has a boxed warning regarding cardiomyopathy. Phesgo administration can result in subclinical and clinical cardiac failure manifesting as congestive heart failure (CHF), and decreased left ventricular ejection fraction (LVEF). The incidence and severity was highest in patients receiving Phesgo with anthracycline-containing chemotherapy regimens. Cardiac function should be evaluated prior to and during treatment with Phesgo. Phesgo has not been studied in patients with a pretreatment LVEF value of < 55% in early breast cancer and < 50% in metastatic breast cancer (1).

Phesgo should be completed 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. In the treatment of metastatic breast cancer, Phesgo should be administered until disease progression or unmanageable toxicity (1).

Phesgo also carries a boxed warning for embryo-fetal toxicity. Exposure to Phesgo can result in embryo-fetal death and birth defects. Females of reproductive potential should be advised to use effective contraception during treatment and for 7 months following the last dose of Phesgo (1).

Phesgo has a third boxed warning about pulmonary toxicity. Phesgo administration can result in serious and fatal pulmonary toxicity. Phesgo should be discontinued for anaphylaxis, interstitial pneumonitis, or acute respiratory distress syndrome. Patients should be monitored until symptoms completely resolve (1).

The safety and effectiveness of Phesgo in pediatric patients have not been established (1).

Related policies
Enhertu, Herceptin Hylecta, Kadcyla, Margenza, Nerlynx, Perjeta, Trastuzumab, Tukysa, Tykerb

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Phesgo may be considered **medically necessary** if the conditions indicated below are met.

Phesgo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Metastatic HER2-positive breast cancer
    a. Used in combination with docetaxel
    b. Patient does **NOT** have a history of prior anti-HER2 therapy or chemotherapy for metastatic disease

2. Neoadjuvant treatment for HER2-positive, locally advanced, inflammatory, or early stage breast cancer
    a. Used in combination with chemotherapy
    b. Greater than 2 cm in diameter **OR** node positive

3. Adjuvant treatment for HER2-positive early breast cancer
    a. Used in combination with chemotherapy

AND ALL of the following:

a. HER2 protein overexpression or HER2 gene amplification as confirmed by an FDA-approved test
b. Left ventricular ejection fraction (LVEF) ≥ 50%
c. Prescriber agrees to monitor cardiac function and monitor for pulmonary toxicity
d. **NOT** used intravenously
e. Will be administered by a healthcare professional
f. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for 7 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Metastatic HER2-positive breast cancer
    a. Used in combination with docetaxel
    b. Left ventricular ejection fraction (LVEF) ≥ 50%
    c. **NO** disease progression or unacceptable toxicity
    d. **NOT** used intravenously
    e. Will be administered by a healthcare professional
    f. Prescriber agrees to monitor cardiac function and monitor for pulmonary toxicity
    g. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for 7 months after the last dose

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Quantity 4 injections every 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity 4 injections every 84 days

Duration 12 months

NO renewal for locally advanced, inflammatory, or early breast cancer

Rationale

Summary

Phesgo is a combination of pertuzumab and trastuzumab, HER2/neu receptor antagonists, and hyaluronidase, an endoglycosidase. Pertuzumab blocks ligand-dependent heterodimerization of HER2 with other HER family members, including EGFR, HER3, and HER4. Trastuzumab inhibits HER2 mediated cell proliferation and PI3K signaling pathway in human cells that overexpress HER2. Both pertuzumab and trastuzumab-mediated antibody-dependent cell-mediated cytotoxicity have been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. The safety and effectiveness of Phesgo in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Phesgo while maintaining optimal therapeutic outcomes.

References

1. Phesgo [package insert]. South San Francisco, CA: Genentech, Inc.; November 2024.
2. NCCN Drugs & Biologics Compendium® Pertuzumab, trastuzumab, and hyaluronidase-zzxf 2026. National Comprehensive Cancer Network, Inc. Accessed on January 12, 2026.

Policy History

Date	Action
August 2020	Addition to PA
September 2020	Annual review
December 2020	Annual review
June 2021	Annual review and reference update
September 2022	Annual review and reference update
June 2023	Annual review and reference update
March 2024	Annual review and reference update
June 2024	Annual review and reference update
March 2025	Annual review and reference update
June 2025	Annual review and reference update
March 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.