Clinical Policy: Pertuzumab/Trastuzumab/Hyaluronidase-zzxf (Phesgo)

Reference Number: ERX.SPA.409
Effective Date: 09.01.20
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Pertuzumab/trastuzumab/hyaluronidase-zzxf (Phesgo™) is a fixed-dose subcutaneous formulation of human epidermal growth factor 2 (HER2)/neu receptor antagonists [Perjeta® (pertuzumab) and Herceptin® (trastuzumab)] and endoglycosidase (hyaluronidase).

FDA Approved Indication(s)
Phesgo is indicated for:

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

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Phesgo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Diagnosis of HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as combination therapy (*see Appendix B*);
5. Request meets one of the following (a or b):*
   a. Dose does not exceed an initial dose of 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase (one single-dose vial), followed by 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase (one single-dose vial) every three weeks;
   b. Dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Breast Cancer (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Phesgo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase (one single-dose vial) every three weeks;
   b. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months (*total of 18 cycles for neoadjuvant or adjuvant therapy*)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER2: human epidermal growth factor 2
MBC: metastatic breast cancer

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of drugs that may be used with Phesgo for breast cancer: • Chemotherapeutic agents: carboplatin, cyclophosphamide, doxorubicin • HER2-targeted agents: docetaxel (Taxotere®), paclitaxel • Endocrine therapy: tamoxifen; aromatase inhibitors: anastrozole (Arimidex®), letrozole (Femara®), exemestane (Aromasin®).	Regimens are dependent on a variety of factors including menopausal status, treatment/progression history, clinical stage, histology, mutational and receptor status, treatment purpose (e.g., adjuvant and neoadjuvant treatment, treatment for metastatic disease).	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to pertuzumab, or trastuzumab, or hyaluronidase, or to any of its excipients
- Boxed warning(s): cardiomyopathy, embryo-fetal toxicity, and pulmonary toxicity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	Initial dose of 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase administered SC in the thigh, followed by maintenance dose of 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase administered SC in the thigh every 3 weeks • *For neoadjuvant*: administer with chemotherapy by IV infusion preoperatively for 3 to 6 cycles for a total of one year (up to 18 cycles) • *For adjuvant*: administer with chemotherapy by IV infusion postoperatively for a total of one year (up to 18 cycles) • *For metastatic disease*: administer with IV infusion of docetaxel Must be administered by a healthcare professional.	See regimens

VI. Product Availability

Single-dose vial for injection:
- 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

VII. References

1. Phesgo Prescribing Information. South San Francisco, CA: Genentech, Inc.; June 2020. Available at: https://www.phesgo.com/hcp.html. Accessed May 5, 2021.
2. Tan AR, Im SA, Mattar A, et al. Abstract PD4-07: 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. *Cancer Res*. 2020; 80(4): PD4-07; doi: 10.1158/1538-7445.SABCS19-PD4-07.
3. National Comprehensive Cancer Network Guidelines. Breast Cancer Version 4.2021. Available at www.nccn.org. Accessed May 5, 2021.
4. National Comprehensive Cancer Network Guidelines. Colon Cancer Version 4.2020. Available at www.nccn.org. Accessed July 8, 2020.
5. National Comprehensive Cancer Network Guidelines. Rectal Cancer Version 6.2020. Available at www.nccn.org. Accessed July 8, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.21.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	05.05.21	08.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional

medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.