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

Reference Number: LA.PHAR.501
Effective Date: 09.29.23
Last Review Date: 02.03.25 ~~04.05.24~~ Coding Implications
Line of Business: Medicaid Revision Log

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

****Please note: This policy is for medical benefit****

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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 received 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.

It is the policy of Louisiana Healthcare Connections® 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 in combination with chemotherapy (*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 guidelines 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53~~ for Medicaid~~.

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit, 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 use of Phesgo as neoadjuvant therapy, the member has not already received more than 6 cycles of therapy;
4. If request is for use of Phesgo as adjuvant therapy, the member has not already received more than 18 cycles of therapy;
5. 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 guidelines 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 ~~(12 months total [18 cycles] *if neoadjuvant or adjuvant therapy*)~~

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53~~ for Medicaid~~.

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 policies – LA.PMN.53 ~~for Medicaid 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
NCCN: National Comprehensive Cancer Network

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 for all relevant lines of business~~ 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	See regimens

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Indication	Dosing Regimen	Maximum Dose
	trastuzumab, and 20,000 units hyaluronidase administered SC in the thigh every 3 weeks • *For neoadjuvant*: administer by SC injection with chemotherapy by IV infusion preoperatively for 3 to 6 cycles for a total of one year • *For adjuvant*: administer by SC injection 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.	

VI. Product Availability

Single-dose ~~vial~~vials for injection:

- 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase per 15 mL **(**80 mg, 40 mg, and 2,000 units/mL)
- 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase per 10 mL (60 mg, 60 mg, and 2,000 units/mL)

VII. References

1. Phesgo Prescribing Information. South San Francisco, CA: Genentech, Inc.; June 2020. Available at: https://www.phesgo.com/hcp.html. Accessed ~~April 20, 2023~~May 23, 2024.
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.~~2023~~2024. Available at: www.nccn.org. Accessed May 22, ~~2023~~2024.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 23, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

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CLINICAL POLICY
Pertuzumab/Trastuzumab/Hyaluronidase-zzxf

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	08.28.23
Annual review; for Continued Therapy added criteria to document whether Phesgo is being used as neoadjuvant or adjuvant therapy in order to determine the appropriate total treatment duration; references reviewed and updated.	04.05.24	07.10.24
Annual review: no significant changes; references reviewed and updated.	02.03.25	

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. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to

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recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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