RXADVANCE
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Clinical Policy Title:	Pertuzumab;Trastuzumab; Hyaluronidase-zzxf
Policy Number:	RxA.639
Drug(s) Applied:	Phesgo™
Original Policy Date:	07/13/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Phesgo (pertuzumab, trastuzumab, and hyaluronidase-zzxf)	Breast cancer (Initial dose)	Initial dose: 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase administered SC over approx. 8 min followed by 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase administered SC over approx. 5min every 3 weeks	600 mg /600 mg every 3 weeks
	Breast cancer (Neoadjuvant & adjuvant)	**Neoadjuvant:** by SC injection every 3 weeks & chemotherapy by intravenous infusion preoperatively for 3 to 6 cycles. (Refer to the prescribing information for pertuzumab, administered in combination with trastuzumab and chemotherapy, for recommended dose) **Adjuvant :** Give Phesgo SC injection every 3 weeks & chemotherapy by intravenous infusion postoperatively for a total of 1 year (up to 18 cycles)	Every 3 weeks

	Metastatic Breast cancer	Give Phesgo SC injection and docetaxel by intravenous infusion every 3 weeks.	Every 3 weeks

Dosage Forms

- Injection:
  - 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase/15 mL (80 mg, 40 mg, and 2,000 units/mL) of solution in a single-dose vial.
  - 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase/10 mL (60 mg, 60 mg, and and 2,000units/mL) of solution in a single-dose vial.

Clinical Policy

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

I. Initial Approval Criteria

A. Breast cancer

1. Diagnosis of HER2 positive breast cancer (early or metastatic);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Phesgo is being prescribed for one of the following (a, b or c):
   a. Given in combination of chemotherapy (must meet i or ii):
      i. as neoadjuvant treatment for adult members 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
      ii. as adjuvant treatment for adult members with HER2-positive early breast cancer at high risk of recurrence
   b. Given in combination with docetaxel for the treatment of adult members with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or
   c. Given with chemotherapy for metastatic disease
5. Request meets one of the following (a or b):
   a. Dose does not exceed initial dose 1200 mg/600 mg; Maintenance dose 600 mg/600 mg every 3 weeks
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months
(For post-surgery or adjuvant treatment, treatment is needed up to 18 cycles or until disease recurrence or unmanageable toxicity, whichever occurs first; For metastatic treatment, treatment is needed until disease progression or unmanageable toxicity, whichever occurs first.)

II. Continued Therapy Approval

A. HER 2 positive Breast Cancer

1. Member is currently receiving medication that has been authorized by RxAdvance 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 the request if for dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 600 mg/600 mg every 3 weeks
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months
(For post-surgery or adjuvant treatment, treatment is needed up to 18 cycles or until disease recurrence or unmanageable toxicity, whichever occurs first; For metastatic treatment, treatment is needed until disease progression or unmanageable toxicity, whichever occurs first.)

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER: human epidermal growth factor receptor
NCCN: National Comprehensive Cancer Network
HER2: Human epidermal growth receptor 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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Perjeta® (pertuzumab)	The initial dose is 840 mg administered as a 60-minute IV infusion, followed every 3 weeks thereafter by 420 mg administered as a 30 to 60 minute IV infusion. MBC: Administer PERJETA, trastuzumab or trastuzumab hyaluronidaseoysk, and docetaxel every 3 weeks. (2.2) Neoadjuvant: Administer PERJETA, trastuzumab or trastuzumab hyaluronidase-oysk, and chemotherapy preoperatively every 3 weeks for 3 to 6 cycles. (2.2) Adjuvant: Administer PERJETA, trastuzumab or trastuzumab hyaluronidase-oysk, and chemotherapy postoperatively every 3 weeks for a total of 1 year (up to 18 cycles)	Refer to Perjeta prescribing information

Herceptin® (trastuzumab) Ogivri™ (trastuzumab- dkst) Ontruzant® (Trastuzumab- dttb) Herzuma® (Trastuzumab- pkrb) Trazimera™ (Trastuzumab- qyyp) Kanjinti™ (Trastuzumab- anns)	Administer according to one of the following doses and schedules for a total of 52 weeks: <u>Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:</u> During and following paclitaxel, docetaxel, or docetaxel/carboplatin: • Initial dose of 4 mg/kg as an IV infusion over 90 minutes then at 2 mg/kg as an IV infusion over 30 minutes weekly during chemotherapy for the first 12 weeks (paclitaxel or docetaxel) or 18 weeks (docetaxel/carboplatin). • One week following the last weekly dose of the trastuzumab product, administer trastuzumab product at 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks. <u>Herceptin, Ogivri, Ontruzant, Trazimera, Kanjinti:</u> As a single agent within 3 weeks following completion of multi-modality, anthracycline based chemotherapy regimens: • Initial dose: 8 mg/kg as an IV infusion over 90 minutes. • Subsequent doses: 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks	Refer to respective prescribing information
Herceptin Hylecta™ (Trastuzumab-hyaluronidase- oysk)	<u>Herceptin Hylecta (subcutaneous product):</u> As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; as part of a treatment regimen with docetaxel and carboplatin; as a single agent following multi-modality anthracycline based therapy: 600 mg trastuzumab and 10,000 units hyaluronidase administered subcutaneously over approximately 2-5 minutes once every 3 weeks	600 mg/10,000 units every 3 weeks

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):
  - Hypersensitivity to pertuzumab, trastuzumab, hyaluronidase, or any component of the formulation.

- Boxed Warning(s):
  - Cardiomyopathy
  - Embryo-fetal toxicity
  - Pulmonary toxicity

APPENDIX D: General Information

- Per NCCN guidelines for breast cancer, Phesgo for subcutaneous use may be substituted anywhere that the

combination of intravenous pertuzumab and intravenous trastuzumab are given as part of systemic therapy. Phesgo is 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.
- Do not substitute Phesgo for or with pertuzumab, trastuzumab, ado-trastuzumab emtansine, or fam-trastuzumab deruxtecan.
- Phesgo must always be administered by a healthcare professional.

References

1. Phesgo Prescribing Information. South San Francisco, CA. Genentech, Inc. June,2020; Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761170s000lbl.pdf. Accessed July 14, 2020.
2. Phesgo. Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 14, 2020.
3. Phesgo NCCN Guidelines (version-5.2020). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Accessed July 15,2020

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	07/14/2020	09/14/2020

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