Clinical Policy Title:	pertuzumab, trastuzumab, hyaluronidase-zzxf
Policy Number:	RxA.639
Drug(s) Applied:	Phesgo™
Original Policy Date:	09/14/2020
Last Review Date:	09/14/2021
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 (Neoadjuvant)	Administer 3-6 cycles for early breast cancer Initial dose: 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase administered subcutaneous over approx. 8 minutes followed by maintenance dosing 3 weeks later Maintenance Dose: 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase administered subcutaneous over approx. 5 minutes every 3 weeks	1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase subcutaneous/dose
	Breast Cancer (Adjuvent)	Initial dose: 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase administered subcutaneous followed by maintenance dosing 3 weeks later Maintenance Dose: 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase subcutaneously once every three weeks	

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Metastatic Breast Cancer	Administer Phesgo™ subcutaneously in combination with docetaxel Initial loading dose: pertuzumab 1,200 mg/trastuzumab 600 mg/hyaluronidase 30,000 units initially, followed 3 weeks later by maintenance dosing. Maintenance dosing: pertuzumab 600 mg/trastuzumab 600 mg/hyaluronidase 20,000 units once 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 2,000 units/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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. HER-2 positive Breast Cancer (must meet all)**:**

1. Diagnosis of HER-2 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 (must meet all):

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 is 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
HER: human epidermal growth factor receptor
NCCN: National Comprehensive Cancer Network
HER-2: Human epidermal growth receptor 2
MBC: Metastatic Breast Cancer

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Perjeta®	The initial dose is 840 mg administered as a 60-minutes intravenous infusion, followed every 3 weeks thereafter by 420 mg administered as a 30-to-60-minutes intravenous infusion. MBC: Administer Perjeta®, trastuzumab or trastuzumab hyaluronidase- oysk , and docetaxel every 3 weeks.	Refer to Perjeta® prescribing information

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Neoadjuvant: Administer Perjeta®, trastuzumab or trastuzumab hyaluronidase-oysk, and chemotherapy preoperatively every 3 weeks for 3 to 6 cycles. Adjuvant: Administer Perjeta®, trastuzumab or trastuzumab hyaluronidase-oysk, and chemotherapy postoperatively every 3 weeks for a total of 1 year (up to 18 cycles)	
Herceptin®, Ogivri™, Ontruzant®, Herzuma®, Trazimera™, Kanjinti™	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 intravenous infusion over 90 minutes then at 2 mg/kg as an intravenous 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 intravenous 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 intravenous infusion over 90 minutes. • Subsequent doses: 6 mg/kg as an intravenous infusion over 30 to 90 minutes every 3	Refer to respective prescribing information

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	weeks	
Herceptin Hylecta™	Herceptin Hylecta™ (subcutaneous product): 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 generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

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.phesgo.com/. Accessed July 05, 2021.

2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org. Accessed July 05, 2021.
3. Breast Cancer (Version 4.2021) National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed July 05, 2021.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com. Accessed July 05, 2021.
5. Pertuzumab, Trastuzumab, and Hyaluronidase, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 05, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	07/14/2020	09/14/2020
Policy was reviewed: 1. Dosing Information first indication was updated from “Breast Cancer (Initial dose)” to “Breast Cancer (Neoadjuvant)”. 2. Dosing information second indication was updated from “Breast Cancer (Neoadjuvant & Adjuvant)” to “Breast Cancer (Adjuvant)”. 3. Dosing Information for indication Breast Cancer (Neoadjuvant) was updated to include “Administer 3-6 cycles for early breast cancer” and “followed by maintenance dosing 3 weeks later; Maintenance Dose:”. 4. Dosing Information for indication Breast Cancer (Adjuvant) was updated to include “Initial dose: 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase administered subcutaneous followed by maintenance…”. 5. Dosing Information for indication Metastatic Breast Cancer was updated to include “Initial loading dose: pertuzumab 1,200 mg/trastuzumab 600 mg/hyaluronidase 30,000 units initially, followed 3 weeks later by maintenance dosing. Maintenance dosing…”. 6. Dosing Information maximum dose was updated from “600mg every 3 weeks” to “1,200 mg pertuzumab,	07/05/2021	09/14/2021

600 mg trastuzumab, and 30,000 units hyaluronidase subcutaneous/dose…". 7. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 8. Initial Approval Criteria I.A was updated from "Breast Cancer" to "HER-2 positive Breast Cancer (must meet all)…" 9. Appendix A was updated to remove abbreviation FDA. 10. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 11. Appendix B: Therapeutic Alternatives was updated to remove inactive/unavailable drug names pertuzumab, trastuzumab, trastuzumab dkst, trastuzumab dttb, trastuzumab pkrb, trastuzumab qyyp, trastuzumab anns, and trastuzumab hyaluronidase oysk. 12. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 13. References were reviewed and updated.		