Clinical Policy: Trastuzumab/Biosimilars, Trastuzumab-Hyaluronidase

Reference Number: PA.CP.PHAR.228
Effective Date: 01/18
Last Review Date: 04/19

Revision Log

Description

- Trastuzumab (Herceptin®) is a human epidermal growth factor receptor 2 (HER2)/neu receptor antagonist.
- Trastuzumab-dkst (Ogivri™), trastuzumab-pkrb (Herzuma®), and trastuzumab-dttb (Ontruzant®) are Herceptin biosimilars.
- Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta™) is a combination of trastuzumab and hyaluronidase, an endoglycosidase.

FDA Approved Indication(s)

Indications*	Description		Herceptin, Ogivri, Ontruzant	Herzuma	Herceptin Hylecta
Adjuvant breast cancer	For adjuvant treatment of HER2-overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer:	As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel	X	X	X
		As part of a treatment regimen with docetaxel and carboplatin	X	X	X
		As a single agent following multi-modality anthracycline based therapy	X	–	X
Metastatic breast cancer	In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer		X	X	X
	As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease		X	X	X
Gastric cancer	In combination with cisplatin and capecitabine or 5-fluorouracil for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction (esophagogastric junction; EGJ)		X	–	–

Indications*	Description	Herceptin, Ogivri, Ontruzant	Herzuma	Herceptin Hylecta
	adenocarcinoma who have not received prior treatment for metastatic disease			

*Select patients for therapy based on an FDA-approved companion diagnostic for trastuzumab.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness® that Herceptin 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. Request meets one of the following (a, b, c, or d):
   a. Herceptin, Ogivri, Herzuma, Ontruzant: dose does not exceed 8 mg/kg IV for adjuvant therapy or 4 mg/kg IV for treatment of metastatic disease;
   b. Herceptin, Ogivri, Herzuma, Ontruzant: intrathecal administration for leptomeningeal metastasis;
   c. Herceptin Hylecta: dose does not exceed 600 mg/10,000 units SC every 3 weeks;
   d. Dose/product is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Gastric, Esophageal and Esophagogastric Junction Cancer (must meet all):
1. Diagnosis of HER2-positive metastatic gastric, esophageal, or EGJ adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with cisplatin and either capecitabine or 5-fluorouracil;
5. Request meets one of the following (a or b):
   a. Herceptin, Ogivri, Ontruzant: dose does not exceed 8 mg/kg IV;
   b. Dose/product is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

C. Endometrial Carcinoma (off-label) (must meet all):
1. Diagnosis of HER2-positive endometrial carcinoma with serous histology;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is advanced (i.e., stage III/IV) or recurrent;
5. Prescribed in combination with carboplatin and paclitaxel;

6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Documentation of positive response to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. Breast cancer (i, ii, or iii):
      i. Herceptin, Ogivri, Herzuma, Ontruzant: new dose does not exceed 8 mg/kg IV for adjuvant therapy or 4 mg/kg IV for treatment of metastatic disease;
      ii. Herceptin, Ogivri, Herzuma, Ontruzant: intrathecal administration for leptomeningeal metastases;
      iii. Herceptin Hylecta: new dose does not exceed 600 mg/10,000 units SC every 3 weeks;
   b. Gastric, esophageal, EGJ cancer: Herceptin, Ogivri, Ontruzant: new dose does not exceed 8 mg/kg IV;
   c. New dose/product is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
EGJ: esophagogastric junction
HER2: human epidermal growth factor receptor 2

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported

- Boxed warning(s):
  - Herceptin, Ogivri, Herzuma, Ontruzant: cardiomyopathy, infusion reactions, embryo-fetal toxicity, pulmonary toxicity
  - Herceptin Hylecta: cardiomyopathy, embryo-fetal toxicity, pulmonary toxicity

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Trastuzumab (Herceptin) Trastuzumab-dkst (Ogivri) Trastuzumab-dttb (Ontruzant) Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta)	Adjuvant treatment, breast cancer	Administer according to one of the following doses and schedules for a total of 52 weeks: ***Herceptin, Ogivri, Herzuma, Ontruzant*** 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. ***Herceptin, Ogivri, Herzuma:*** 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	8 mg/kg
		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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Trastuzumab (Herceptin), Trastuzumab-dkst (Ogivri)	Metastatic treatment, breast cancer	***Herceptin, Ogivri, Herzuma, Ontruzant:*** As a single agent, or in combination with paclitaxel, at an initial dose of 4 mg/kg as a 90-minute intravenous infusion followed by subsequent once weekly doses of 2 mg/kg as 30-minute intravenous infusions until disease progression.	4 mg/kg
		Herceptin Hylecta (subcutaneous product): As a single agent or in combination with paclitaxel: 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
Trastuzumab (Herceptin), Trastuzumab-dkst (Ogivri), Trastuzumab-dttb (Ontruzant)	Metastatic gastric cancer	***Herceptin, Ogivri, Ontruzant:*** Administer at an initial dose of 8 mg/kg as a 90 minute intravenous infusion followed by subsequent doses of 6 mg/kg as an intravenous infusion over 30 to 90 minutes every three weeks until disease progression.	8 mg/kg

V. Product Availability

Drug Name	Availability*
Trastuzumab (Herceptin)	Multi-use vial: 420 mg Single-dose vial: 150 mg
Trastuzumab-dkst (Ogivri)	Multi-use vial: 420 mg
Trastuzumab-pkrb (Herzuma)	Multi-use vial: 420 mg
Trastuzumab-dttb (Ontruzant)	Single-dose vial: 150 mg
Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta)	Single-dose vial: 600 mg (trastuzumab)/10,000 units (hyaluronidase)/5 mL

*All products are supplied as a powder for reconstitution with the exception of Herceptin Hylecta which is supplied as a solution.

VI. References

1. Herceptin Prescribing Information. South San Francisco, CA: Genentech, Inc.; November 2018. Available at http://www.gene.com/download/pdf/herceptin_prescribing.pdf. Accessed March 5, 2019.
2. Ogivri Prescribing Information. Morgantown, WV: Mylan GmbH.; December 2017. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761074s000lbl.pdf. Accessed March 5, 2019.

3. Herzuma Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2018. https://www.herzuma.com/globalassets/herzuma/herzuma-pi.pdf. Accessed March 5, 2019.
4. Ontruzant Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; January 2019. https://www.merck.com/product/usa/pi_circulars/o/ontruzant/ontruzant_pi.pdf. Accessed March 5, 2019.
5. Herceptin Hyclecta Prescribing Information. South San Francisco, CA: Genentech, Inc.; February 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761106s000lbl.pdf. Accessed March 5, 2019.
6. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 7, 2019.
7. National Comprehensive Cancer Network. Breast Cancer Version 3.2018. Available at: http://www.nccn.org. Accessed February 7, 2019.
8. National Comprehensive Cancer Network. Gastric Cancer Version 2.2018. Available at: http://www.nccn.org. Accessed February 7, 2019.
9. National Comprehensive Cancer Network. Uterine Neoplasms Version 2.2019. Available at: http://www.nccn.org. Accessed February 7, 2019.
10. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2018. Available at: http://www.nccn.org. Accessed February 7, 2019.

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
J9355	Injection, trastuzumab, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date
1Q2018 annual review. Ogivri added. Age, specialist and dosing added. Breast cancer criteria sets combined; criteria limited to a diagnosis of HER2+ breast cancer. CNS breast cancer metastatic disease off-label criteria limited to diagnosis. Off-label uses removed from gastric cancer criteria - FDA indications cover through NCCN category 2A. HER2-positive lung cancer removed as an off-label indication per NCCN. References reviewed and updated.	1.16.18	
2Q 2019 annual review: Herceptin biosimilars and Herceptin combination product added (biosimilars - Herzuma, Ontruzant; combination product -	04/19	

Reviews, Revisions, and Approvals	Date	Approval Date
Herceptin Hylecta); intrathecal treatment for breast cancer related CNS metastasis is moved to the breast cancer criteria set; NCCN recommended use for endometrial carcinoma are added; references reviewed and updated.		