Clinical Policy: Trastuzumab/Biosimilars, Trastuzumab-Hyaluronidase

Reference Number: ERX.SPA.42
Effective Date: 07.01.16
Last Review Date: 05.20
Line of Business: Commercial, Medicaid

Revision Log

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

Description

- Trastuzumab (Herceptin®) is a human epidermal growth factor receptor 2 (HER2)/neu receptor antagonist.
- Trastuzumab-dkst (Ogivri™), trastuzumab-pkrb (Herzuma®), trastuzumab-dttb (Ontruzant®), trastuzumab-qyyp (Trazimera™), and trastuzumab-anns (Kanjinti™) 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, Trazimera, Kanjinti	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	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) adenocarcinoma who have not received prior treatment for metastatic disease		X	X	–

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

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 Herceptin/biosimilars and Herceptin Hylecta are **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 or leptomeningeal metastases from 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, Trazimera, Kanjinti: Dose does not exceed 8 mg/kg IV for adjuvant therapy or 4 mg/kg IV for treatment of metastatic disease (*see Appendix D for dose rounding guidelines);*
   b. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: Intrathecal administration for leptomeningeal metastasis;
   c. Herceptin Hylecta: Dose does not exceed 600 mg/10,000 units SC every 3 weeks (*see Appendix D for dose rounding guidelines);*
   d. Dose/product 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. 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;*
   **Prior authorization may be required.*
5. Request meets one of the following (a or b):*
   a. Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti: Dose does not exceed 8 mg/kg IV (*see Appendix D for dose rounding guidelines);*
   b. Dose/product 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

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;*
   **Prior authorization may be required.*
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*).*

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

Approval duration: 6 months

D. Colorectal Cancer (off-label) (must meet all):
1. Diagnosis of advanced or metastatic colorectal cancer and both of the following (a and b):
    1. Disease is HER2 positive;
    2. Disease is wild-type *RAS* (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. No previous use of a HER2 inhibitor therapy (e.g., trastuzumab, Kadcyla®, Tykerb®, Perjeta®);
5. Prescribed in combination with Perjeta (pertuzumab) or Tykerb (lapatinib);*
   **Prior authorization may be required.*
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*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

E. 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. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Herceptin 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, b, or c):*
    a. Breast cancer (i, ii, or iii):
        i. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: New dose does not exceed 8 mg/kg IV for adjuvant therapy or 4 mg/kg IV for treatment of metastatic disease (*see Appendix D for dose rounding guidelines);*
        ii. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: Intrathecal administration for leptomeningeal metastasis;
        iii. Herceptin Hylecta: New dose does not exceed 600 mg/10,000 units SC every 3 weeks (*see Appendix D for dose rounding guidelines);*
    b. Gastric, esophageal, EGJ cancer: Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti: New dose does not exceed 8 mg/kg IV (*see Appendix D for dose rounding guidelines);*
    c. New dose/product 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

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
EGJ: esophagogastric junction
HER2: human epidermal growth factor receptor 2
KRAS: Kirsten rat sarcoma 2 viral oncogene homologue
NRAS: neuroblastoma RAS viral oncogene homologue

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: cardiomyopathy, infusion reactions, embryo-fetal toxicity, pulmonary toxicity
  - Herceptin Hylecta: cardiomyopathy, embryo-fetal toxicity, pulmonary toxicity

Appendix D: Dose Rounding Guidelines

Weight-based Dose Range	Vial Quantity Recommendation
≤ 157.49 mg	1 vial of 150 mg
157.5 mg-314.99 mg	2 vials of 150 mg
315 mg-440.99 mg	1 vial of 420 mg
441 mg-598.49 mg	1 vial of 150 mg and 1 vial 420 mg
598.5 mg-881.99 mg	2 vials of 420 mg
882 mg-1,039.49 mg	1 vial of 150 mg and 2 vials of 420 mg
1,039.5 mg-1,322.99 mg	3 vials of 420 mg

V. Dosage and Administration

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

Drug Name	Indication	Dosing Regimen	Maximum Dose
		• Subsequent doses: 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks	
		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
Trastuzumab (Herceptin) Trastuzumab-dkst (Ogivri) Trastuzumab-dttb (Ontruzant) Trastuzumab-pkrb (Herzuma) Trastuzumab-qyyp (Trazimera) Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta) Trastuzumab-anns (Kanjinti)	Metastatic treatment, breast cancer	***Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:*** 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) Trastuzumab-qyyp (Trazimera) Trastuzumab-anns (Kanjinti)	Metastatic gastric cancer	***Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti:*** 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

VI. Product Availability

Drug Name	Availability*
Trastuzumab (Herceptin)	Multi-dose vial: 440 mg Single-dose vial: 150 mg
Trastuzumab-dkst (Ogivri)	Multi-dose vial: 420 mg Single-dose vial: 150 mg
Trastuzumab-pkrb (Herzuma)	Multi-dose vial: 420 mg Single-dose vial: 150 mg
Trastuzumab-dttb (Ontruzant)	Single-dose vial: 150 mg

Drug Name	Availability*
	Multi-dose vial: 420 mg
Trastuzumab-qyyp (Trazimera)	Multi-dose vial: 420 mg
Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta)	Single-dose vial: 600 mg (trastuzumab)/10,000 units (hyaluronidase)/5 mL
Trastuzumab-anns (Kanjinti)	Multi-dose vial: 420 mg

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

VII. References

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6. 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 February 17, 2020.
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10. National Comprehensive Cancer Network. Gastric Cancer Version 4.2019. Available at: http://www.nccn.org. Accessed February 17, 2020.
11. National Comprehensive Cancer Network. Uterine Neoplasms Version 5.2019. Available at: http://www.nccn.org. Accessed February 17, 2020.
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13. Fahrenbruch R, Kintzel P, Bott AM., et al. Dose rounding of biologic and cytotoxic anticancer agents: a position statement of the hematology/oncology pharmacy association. Journal of Oncology Practice. 2018;14(3)e130-e136.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.16	06.16
Increased approval durations from 3/6 months to 6/12 months. Removed non-small cell lung cancer off-label NCCN use as it is a 2B recommendation.	04.17	05.17
Policy converted to new template. Age, specialist and dosing added. Breast cancer criteria sets combined; criteria limited to a diagnosis of HER2+ breast cancer.	01.16.18	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.		
2Q 2018 annual review: no significant changes; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: Herceptin biosimilars and Herceptin combination product added (biosimilars - Ogivri, Herzuma, Ontruzant, Trazimera; combination product - 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.	03.19.19	05.19
Added new Ogivri formulation: 150 mg single-dose vial.	05.08.19	
RT4: added new Ogivri formulation: 150 mg single-dose vial; added Herceptin biosimilar: Kanjinti; added newly FDA-approved indication for gastric cancer and new 150 mg vial formulation for Herzuma; references updated.	06.18.19	
Herceptin product availability for multi-dose vial corrected from 420 mg to 440 mg; references updated.	08.12.19	
2Q 2020 annual review: added NCCN compendium-supported indications of colon and rectal cancer; incorporated NCCN compendium-supported indication of leptomeningeal metastases from HER2-positive breast cancer into breast cancer criteria; added new Ontruzant formulation of 420 mg multidose vial; added appendix D: dose rounding guidelines; added reference to appendix D within criteria; references reviewed and updated.	02.17.20	05.20

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.