

Clinical Policy: Trastuzumab/Biosimilars, Trastuzumab-Hyaluronidase

Reference Number: CP.PHAR.228

Effective Date: 06.01.16

Last Review Date: 05.19

Line of Business: Medicaid, HIM*, HIM-Medical Benefit

[Coding Implications](#)

[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.

**For Health Insurance Marketplace (HIM), if request is via pharmacy benefit, Herceptin 150 mg, Ogivri, Herzuma, Ontruzant, Trazimera, Herceptin Hylecta, and Kanjinti are non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

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
Metastatic breast cancer	In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer	X	X	X	

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Indications*	Description	Herceptin, Ogivri, Ontruzant, Trazimera, Kanjinti	Herzuma	Herceptin Hylecta
	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.

It is the policy of health plans affiliated with Centene Corporation® 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;
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;
 - 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;
 - 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:

Medicaid – 6 months

HIM – 6 months for Herceptin 420 mg (*refer to HIM.PA.103 for Herceptin 150 mg, Ogivri, Herzuma, Ontruzant, Trazimera, Herceptin Hylecta, and Kanjinti*)

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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 \geq 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;
 - 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:

Medicaid – 6 months

HIM – 6 months for Herceptin 420 mg (*refer to HIM.PA.103 for Herceptin 150 mg, Ogivri, Ontruzant, Trazimera, and Kanjinti*)

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 \geq 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*).

Approval duration:

Approval duration:

Medicaid – 6 months

HIM – 6 months for Herceptin 420 mg (*refer to HIM.PA.103 for Herceptin 150 mg, Ogivri, Herzuma, Ontruzant, Trazimera, Herceptin Hylecta, and Kanjinti*)

D. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Approval

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving the requested agent for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;

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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;
 - ii. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: 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, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti: 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:

Medicaid – 12 months

HIM – 12 months for Herceptin 420 mg (*refer to HIM.PA.103 for Herceptin 150 mg, Ogivri, Herzuma, Ontruzant, Trazimera, Herceptin Hylecta, and Kanjinti*)

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

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

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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 – HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid and HIM-Medical Benefit 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

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):

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- Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: cardiomyopathy, infusion reactions, embryo-fetal toxicity, pulmonary toxicity
- Herceptin Hylecta: cardiomyopathy, embryo-fetal toxicity, pulmonary toxicity

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: <u>Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:</u> During and following paclitaxel, docetaxel, or docetaxel/carboplatin: <ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> • 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
		<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

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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)	Metastatic treatment, breast cancer	<u>Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:</u> 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. <u>Herceptin Hylecta (subcutaneous product):</u> 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.	4 mg/kg 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	<u>Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti:</u> 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: 420 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

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Drug Name	Availability*
Trastuzumab-dttb (Ontruzant)	Single-dose vial: 150 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

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.; April 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761074s004lbl.pdf. Accessed May 8, 2019.
3. Herzuma Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; May 2019. <https://www.herzuma.com/globalassets/herzuma/herzuma-pi.pdf>. Accessed June 20, 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. Trazimera Prescribing Information. New York, NY: Pfizer Labs; March 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761081s000lbl.pdf. Accessed March 27, 2019.
6. Herceptin Hylecta 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.
7. Kanjinti Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; June 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761073Orig1s000lbl.pdf. Accessed June 18, 2019.
8. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 7, 2019.
9. National Comprehensive Cancer Network. Breast Cancer Version 3.2018. Available at: <http://www.nccn.org>. Accessed February 7, 2019.
10. National Comprehensive Cancer Network. Gastric Cancer Version 2.2018. Available at: <http://www.nccn.org>. Accessed February 7, 2019.
11. National Comprehensive Cancer Network. Uterine Neoplasms Version 2.2019. Available at: <http://www.nccn.org>. Accessed February 7, 2019.
12. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2018. Available at: <http://www.nccn.org>. Accessed February 7, 2019.

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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	P&T Approval Date
Policy split from CP.PHAR.67.HER2 BrCa Tx and converted to new template. Requests for documentation removed. Reasons for discontinuation limited to absolute requirements per the PI. Definition of adjuvant therapy added to the criteria per NCI definition. NCCN compendial recommended uses added.	05.16	06.16
Initial: Updated off-label NCCN uses for non-metastatic breast cancer (specified disease stages) and metastatic gastric/esophageal adenocarcinomas (added performance score requirement). Re-auth: Removed reasons to discontinue. Added requirement for documentation of positive response to therapy. Increased approval durations from 3 & 6 months to 6 & 12 months. Added Appendix B with definition of performance scores.	04.17	06.17
Policy converted to new template. 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. Removed Appendix B. References reviewed and updated.	01.16.18	02.18
2Q 2018 annual review: no significant changes; HIM line of business added; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: Herceptin biosimilars and Herceptin combination product added (biosimilars - Herzuma, Ontruzant, Trazimera; combination product - Herceptin Hylecta); intrathecal treatment for breast cancer related CNS metastasis is moved	03.19.19	05.19

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
to the breast cancer criteria set; NCCN recommended use for endometrial carcinoma are added; references reviewed and updated.		
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 added; references updated.	06.18.19	

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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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

This clinical policy is the property of the Health Plan. 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.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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