Clinical Policy: Herceptin/Biosimilars, Trastuzumab-Hyaluronidase

Reference Number: AZ.CP.PHAR.228
Effective Date: 04.15.2020
Last Review Date: 04.21
Line of Business: Arizona Medicaid (AzCH-CCP and Care1st)

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.

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		X	X	X

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Indications*	Description	Herceptin, Ogivri, Ontruzant, Trazimera, Kanjinti	Herzuma	Herceptin Hylecta
	chemotherapy regimens for metastatic disease			
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 Arizona Complete Health-Complete Care Plan and Care1st 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 is for a biosimilar (Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti):
   a. Contraindicated or clinically significant adverse effects are experienced to Herceptin;
5. 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 a plantinum agent (i.e., either cisplatin or oxaplatin) and either capecitabine or 5-fluorouracil;*

   **Prior authorization may be required.*
5. Request is for a biosimilar (Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti):
   a. Contraindicated or clinically significant adverse effects are experienced to Herceptin;
6. 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. Request is for a biosimilar (Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti):
   a. Contraindicated or clinically significant adverse effects are experienced to Herceptin;
7. 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):

a. Disease is HER2 positive;
b. 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. Request is for a biosimilar (Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti):
   a. Contraindicated or clinically significant adverse effects are experienced to Herceptin;
7. 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 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): AZ.CP.PMN.53 for Arizona Medicaid.

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;
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 metastases;
      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 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): AZ.CP.PMN.53 for Arizona Medicaid.

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 – AZ.CP.PMN.53 for Arizona Medicaid 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 to 314.99 mg	2 vials of 150 mg
315 mg to 440.99 mg	1 vial of 420 mg
441 mg to 598.49 mg	1 vial of 150 mg and 1 vial 420 mg
598.5 mg to 881.99 mg	2 vials of 420 mg
882 mg to 1,039.49 mg	1 vial of 150 mg and 2 vials of 420 mg
1,039.5 mg to 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. • Subsequent doses: 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks	8 mg/kg

Drug Name	Indication	Dosing Regimen	Maximum Dose
		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),	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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Trastuzumab-qyyp (Trazimera), Trastuzumab-anns (Kanjinti)			

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
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.; February 2021. Available at https://www.gene.com/download/pdf/herceptin_prescribing.pdf. Accessed March 24, 2021.
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3. Herzuma Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; May 2019. https://www.herzuma.com/globalassets/herzuma/herzuma-pi.pdf. Accessed March 24, 2021.
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9. National Comprehensive Cancer Network. Gastric Cancer Version 1.2021. Available at: http://www.nccn.org. Accessed March 24, 2021.
10. National Comprehensive Cancer Network. Uterine Neoplasms Version 5.2019. Available at: http://www.nccn.org. Accessed March 24, 2021.
11. National Comprehensive Cancer Network. Central Nervous System Cancers Version 3.2019. Available at: http://www.nccn.org. Accessed March 24, 2021.
12. 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.

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
J9356	Injection, trastuzumab, 10 mg and hyaluronidase-oysk
Q5112	Injection, trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg
Q5113	Injection, trastuzumab-pkrb, biosimilar, (Herzuma), 10 mg
Q5114	Injection, trastuzumab-dkst, biosimilar, (Ogivri), 10 mg
Q5116	Injection, trastuzumab-qyyp, biosimilar, (Trazimera), 10 mg
Q5117	Injection, trastuzumab-anns, biosimilar, (Kanjinti), 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created to specify Herceptin is the preferred product.	04.20	04.20

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added choice of oxaliplatin, in addition to cisplatin, for combination treatment of gastric cancers per NCCN; references reviewed and updated	04.21	04.21
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21

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.

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.