Clinical Policy: Trastuzumab/Biosimilars, Trastuzumab-Hyaluronidase

Reference Number: CP.PHAR.228
Effective Date: 06.01.16
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

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®), trastuzumab-anns (Kanjinti®), and trastuzumab-strf (Hercessi™) are Herceptin biosimilars.
- Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta™) is a combination of trastuzumab and hyaluronidase, an endoglycosidase.

FDA Approved Indication(s)

Indications*	Description		Herceptin, Hercessi, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti	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
		As part of a treatment regimen with docetaxel and carboplatin	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
	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

Indications*	Description	Herceptin, Hercessi, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti	Herceptin Hylecta
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	–

*Select patients for therapy based on an FDA-approved companion diagnostic for trastuzumab.
** High-risk is defined as ER/PR positive with one of the following features: tumor size > 2 cm, age < 35 years, or tumor grade 2 or 3>

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 or leptomeningeal metastases from HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. If request is for Herceptin, Hercessi, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;

5. Request meets one of the following (a, b, c, or d):*
   a. Herceptin, Ogivri, Herzuma, Hercessi, 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, Hercessi, 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 gastric, esophageal, or EGJ adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is advanced, recurrent, unresectable, or metastatic;
5. Prescribed in combination with systemic chemotherapy;
   **Prior authorization may be required.*
6. If request is for Herceptin, Hercessi, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;

      **Prior authorization may be required*
   b. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;

      **Prior authorization may be required*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
6. Request meets one of the following (a or b):*
   a. Herceptin, Herzuma, Hercessi, 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 one of the following ways (a or b):
   a. In combination with carboplatin and paclitaxel;*
      **Prior authorization may be required.*
   b. As a single agent for maintenance therapy;
6. If request is for Herceptin, Hercessi, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
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 disease is all of the following (a, b, and c):
   a. HER2 positive;
   b. Wild-type *RAS* (defined as wild-type in both KRAS and NRAS [i.e., KRAS and NRAS mutation-negative] as determined by an FDA-approved test for this use);
   c. Wild-type *BRAF* (i.e., BRAF mutation-negative);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. If request is for Herceptin, Hercessi, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*

   b. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
5. Prescribed in combination with Perjeta® (pertuzumab), Tykerb® (lapatinib), or Tukysa® (tucatinib);*
   **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. Salivary Gland Tumor (off-label) (must meet all)**:**
1. Diagnosis of HER2-positive salivary gland tumor;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is recurrent;
5. Prescribed in one of the following manners (a, b, or c):
   a. Single agent;
   b. Combination with docetaxel;*
   c. Combination with Perjeta;*
   **Prior authorization may be required.*
6. If request is for Herceptin, Hercessi, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E);*
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

F. Gallbladder Cancer or Cholangiocarcinoma (off-label) (must meet all):
1. Diagnosis of HER2-positive gallbladder cancer or cholangiocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is unresectable, resected gross residual (R2), or metastatic;
5. Prescribed in combination with Perjeta*;
   **Prior authorization may be required.*
6. If request is for Herceptin, Hercessi, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E);*
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

G. Other diagnoses/indications (must meet all):
1. One of the following (a, b, or c):
   a. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E);*
   b. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*
   c. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*

2. One of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
      ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for 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. For adjuvant breast cancer therapy, member has received ≤ 52 weeks of therapy total;
4. If request is for Herceptin, Hercessi, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (I and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
5. 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, Hercessi, 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, Hercessi, 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, Hercessi, 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 *(total of 52 weeks for adjuvant breast cancer therapy)*

B. Other diagnoses/indications (must meet all)**:**
1. One of the following (a, b, or c):
   a. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E);*
   b. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant, Hercessi, and Herzuma;
      **Prior authorization may be required*
   c. If request is for Herzuma, Hercessi, or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*
2. One of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
      ii. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for 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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BRAF: v-Raf murine sarcoma viral oncogene homolog B1
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, Hercessi: 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

Appendix E: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.

State	Step Therapy Prohibited?	Notes
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
MS	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

Appendix F: General Information

Residual Tumor (R) Classification		
R0	no residual tumor	resected, negative margin
R1	microscopic residual tumor	resected, positive margin
R2	macroscopic residual tumor	resected, gross residual disease

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	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, Hercessi:*** 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.	8 mg/kg

Drug Name	Indication	Dosing Regimen	Maximum Dose
(Herceptin Hylecta), Trastuzumab-anns (Kanjinti), Trastuzumab-strf (Hercessi)		***Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti, Hercessi:*** 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	
		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, Hercessi:*** 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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Trastuzumab-strf (Hercessi)			
Trastuzumab (Herceptin), Trastuzumab-dkst (Ogivri), Trastuzumab-dttb (Ontruzant), Trastuzumab-qyyp (Trazimera), Trastuzumab-anns (Kanjinti), Trastuzumab-strf (Hercessi)	Metastatic gastric cancer	***Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti, Hercessi:*** 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)	Single-dose vial: 150 mg
Trastuzumab-dkst (Ogivri)	Single-dose vial: 150 mg Multi-dose vial: 420 mg**
Trastuzumab-pkrb (Herzuma)	Single-dose vial: 150 mg Multi-dose vial: 420 mg
Trastuzumab-dttb (Ontruzant)	Single-dose vial: 150 mg Multi-dose vial: 420 mg
Trastuzumab-qyyp (Trazimera)	Single-dose vial: 150 mg 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)	Single-dose vial: 150 mg Multi-dose vial: 420 mg
Trastuzumab-strf (Hercessi)	Single-dose vial: 150 mg

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

*** Product available with or without diluent provided*

VII. References

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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
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals
J9355	Injection, trastuzumab, excludes biosimilar, 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
Add the following for all indications per March SDC and prior clinical guidance: 'For requests other than Ogivri or Trazimera, medical justification supports inability to use Ogivri or Trazimera (e.g., contraindications to excipients)'	03.03.20	
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; revised HIM-Medical Benefit line of business and applied HIM line of business to all agents in this policy; added new Ontruzant formulation of 420 mg multidose vial; added appendix D: dose rounding guidelines; added reference to appendix D within criteria; added requirement for medical justification that supports inability to use Ogivri or Trazimera to Section II for continued therapy requests; allowed by-passing of	04.20.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
redirection if state regulations do not allow step therapy in Stage IV or metastatic cancer settings; references reviewed and updated.		
Removed AR from appendix E ("For metastatic cancer, **unless** the preferred drug is consistent with "best practices" (1) used for treatment under (A) FDA-approved indication, or (B) National Comprehensive Cancer Network Drugs & Biologics Compendium; or (2) using evidence-based, peer-reviewed, recognized medical literature. Note – may not require step therapy a second time for same Rx drug") to minimize misinterpretation.	11.16.20	
Updated appendix E to include Ohio	02.08.21	
Updated GA language in appendix E.	03.10.21	
2Q 2021 annual review: revised requirement of medical justification for inability to use preferred Ogivri or Trazimera to "must use" language and applied redirection to preferred biosimilars to other diagnoses/indications; added criteria for salivary gland tumor criteria for Herceptin as it is a NCCN-supported off-label indication; per NCCN support, added wild-type *BRAF* criterion for colorectal cancer and choice of oxaliplatin, in addition to cisplatin, for combination treatment of gastric cancers; updated product availability for Herceptin, Kanjinti, and Trazimera; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	03.25.21	05.21
Per August SDC and prior clinical guidance, modified biosimilar redirection requirements for Herceptin to require use of Ogivri, Trazimera, Kanjinti, Ontruzant and Herzuma in a step-wise manner; for Ontruzant and Herzuma modified redirection to require use of Ogivri, Trazimera, and Kanjinti; for salivary gland tumor indication added redirection to preferred biosimilars per NCCN Compendium; adding legacy Wellcare Medicaid line of business (WCG.CP.PHAR.228 to be retired); added Nevada to Appendix E.	08.25.21	11.21
2Q 2022 annual review: added qualifiers of "advanced" and "recurrent" for gastric, esophageal, or EGJ adenocarcinoma; initial approval durations were consolidated to 6 months for alignment between legacy WCG and other lines of business; removed general description of "stage IV or metastatic" cancer for states with regulations against redirections; clarified other diagnoses section to clarify intent for biosimilar steerage; references reviewed and updated.	02.16.22	05.22
Template changes applied to other diagnoses/indications.	10.10.22	
2Q 2023 annual review: added gallbladder cancer and cholangiocarcinoma as NCCN supported off-label indication; references reviewed and updated.	01.20.23	05.23
Updated Appendix E to include Oklahoma.	06.07.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2024 annual review: for adjuvant breast cancer continued therapy, added member has received ≤ 52 weeks of therapy per PI; for gastric, esophageal, or EGJ, added option for unresectable disease, revised prescribed combination therapy to "systemic chemotherapy" as additional regimens options available per NCCN; for endometrial carcinoma added option to be prescribed as single agent for maintenance therapy per NCCN; for colorectal cancer, removed requirement for no previous use of HER2 inhibitor therapy and added tucatinib as option to be prescribed in combination with; for gallbladder cancer or cholangiocarcinoma, added option for treatment with resected gross residual (R2) disease per NCCN; residual (R) tumor classification added to Appendix F; for Ogivri, updated product availability of 420 mg multi-dose vial supplied with or without diluent; references reviewed and updated.	01.18.24	05.24
RT4: added Hercessi to policy as non-preferred biosimilar. Updated Appendix E to include Mississippi.	06.05.24	

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.