Utilization Review Policy 212B

POLICY: Biosimilars – Herceptin, Herzuma & Ontruzant

- Herceptin® (trastuzumab injection for intravenous infusion – Genentech Inc.)
- Hercessi™ (trastuzumab-strf intravenous infusion – Accord BioPharma)
- Herzuma® (trastuzumab-pkrb injection for intravenous use – Celltrion)
- Ontruzant® (trastuzumab-dttb injection for intravenous use – Merck)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 05/07/2025

COVERAGE CRITERIA FOR: UCare Medicare Plans Only (UCare Medicare, EssentiaCare, Group Plans, MSHO, Connect + Medicare, UCare Your Choice)

OVERVIEW

Trastuzumab products are human epidermal growth factor receptor 2 (HER2)/neu receptor antagonists indicated for the following uses:[1]

- **Breast cancer, adjuvant treatment** of HER2-overexpressing node positive or node negative (estrogen receptor[ER]/progesterone receptor [PR] negative or with one high risk feature) 1) as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; 2) as part of treatment regimen with docetaxel and carboplatin; or 3) as a single agent following multi-modality anthracycline based therapy.
- **Breast cancer, metastatic,** HER2-overexpressing, either in combination with paclitaxel for first-line treatment, or as a single agent in patients who have received one or more chemotherapy regimens for metastatic disease.
- **Gastric cancer or gastroesophageal (GE) junction adenocarcinoma, metastatic**, HER2-overexpressing, in combination with cisplatin and capecitabine or 5-fluorouracil (5-FU) who have not received prior treatment for metastatic disease.

Herzuma, Hercessi, Kanjinti, Ogivri, Ontruzant, and Trazimera are all approved biosimilars for Herceptin; all of the biosimilars have the same FDA-approved indications as Herceptin. For all indications, patients must be selected for therapy based on an FDA-approved companion diagnostic for trastuzumab. Tests are specific for breast cancer or gastric cancer.

Dosing Information

The approved dosing of trastuzumab as *adjuvant treatment of breast cancer* is given for a total of 52 weeks.[1] Initial dose is 4 mg/kg intravenously, then 2 mg/kg weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin). One week after the last weekly dose, trastuzumab 6 mg/kg is given every three weeks to complete a total of 52 weeks of therapy. Another dosing schedule is an initial dose of 8 mg/kg, then 6 mg/kg every 3 weeks for a total of 52 weeks of therapy. Extending adjuvant treatment beyond 1 year is not recommended. The approved dosing for *metastatic breast cancer* is trastuzumab (alone or in combination with paclitaxel) at an initial dose of 4 mg/kg given intravenously followed by weekly doses of 2 mg/kg until disease progression.[1] Many dosing schedules for trastuzumab are included in guidelines.[2] Alternate dosing will be assessed individually on a case-by-case basis.

The approved dose of trastuzumab given with chemotherapy in metastatic gastric cancer is an initial dose of 8 mg/kg intravenously followed by subsequent doses of 6 mg/kg every 3 weeks until progression.[1] Guidelines recommend either trastuzumab 8 mg/kg on Day 1 of Cycle 1 and then 6 mg/kg every 21 days or trastuzumab 6 mg/kg on Day 1 of Cycle 1 and then 4 mg/kg every 14 days for first-line or second-line

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therapy (in combination with chemotherapy) for metastatic or locally advanced gastric, esophageal, or GE junction cancer.[3-4]

For colon cancer or rectal cancer, when used in combination with Perjeta® (pertuzumab intravenous infusion), trastuzumab is given as an 8 mg/kg infusion on Day 1 of Cycle 1 followed by 6 mg/kg every 21 days. When used in combination with lapatinib, trastuzumab is given as a 4 mg/kg infusion on Day 1 of Cycle 1, followed by 2 mg/kg weekly.[5-6]

For biliary tract cancer, endometrial carcinoma and salivary gland tumors, in the clinical studies, trastuzumab 8 mg/kg intravenous infusion followed by 6 mg/kg intravenous infusion not more frequently than once every 3 weeks was given.[7,8, 9]

Guidelines
Trastuzumab is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **Breast Cancer:** NCCN guidelines (version 4.2024 – July 3, 2024) recommend trastuzumab in combination with chemotherapy or endocrine therapy for adjuvant treatment of HER2-positive breast cancer (category 2A).[2,10] Trastuzumab in combination with paclitaxel (category 2A) is a preferred preoperative/adjuvant therapy regimen. The guidelines also list other trastuzumab-containing regimens for preoperative and adjuvant therapy. The preferred first-line agents for HER2-positive recurrent or metastatic disease (either hormone receptor-negative or hormone receptor-positive and refractory to endocrine therapy) include: Perjeta plus trastuzumab plus docetaxel (category 1) or paclitaxel (category 2A). The guidelines list other trastuzumab-containing regimens for HER2-positive metastatic disease.
- **Colon and Rectal Cancer:** NCCN guidelines for colon cancer (version 4.2024 – July 3, 2024) and NCCN guidelines for rectal cancer (version 3.2024 – July 3, 2024) list trastuzumab in combination with Perjeta, Tukysa (tucatinib tablets), or lapatinib tablets in patients with HER2-amplified disease, RAS and BRAF wild-type disease.[3-4,10]
- **Gastric Cancer and Esophageal and Esophagogastric Junction Cancers**: NCCN guidelines for Gastric Cancer (version 2.2024 – May 29, 2024) and Esophageal and Esophagogastric Junction Cancers (version 3.2024 – April 26, 2024) state that for metastatic, locally advanced or recurrent disease (where local therapy is not indicated) trastuzumab should be added to first-line systemic chemotherapy for HER2-overexpressing adenocarcinoma.[5-6,10] The recommended regimens for metastatic or locally advanced HER2-positive gastric, esophageal, or esophagogastric junction adenocarcinoma are trastuzumab in combination with cisplatin or oxaliplatin and a fluoropyrimidine (5-FU or capecitabine) [category 1] or trastuzumab in combination with other chemotherapy agents (category 2A/2B) [various regimens based on individual patient characteristics]. Trastuzumab is not recommended for use in combination with anthracyclines.
- **Head and Neck Cancers:** NCCN guidelines (version 4.2024 – May 1, 2024) recommend trastuzumab as a systemic therapy option for recurrent, unresectable, or metastatic salivary gland tumors, (useful in certain circumstances), for HER2-positive tumors as a single agent or in combination with Perjeta or docetaxel (category 2A).[7,10]
- **Biliary Tract Cancers:** NCCN guidelines (version 3.2024 – July 2, 2024) recommend trastuzumab + Perjeta and trastuzumab + Tukysa as subsequent-line therapy for biliary tract cancers for progression on or after systemic treatment for unresectable or metastatic disease that is HER2-positive (both category 2A).[8,10]
- **Uterine Neoplasms**: NCCN guidelines (version 2.2024 – March 6, 2024) list the combination chemotherapy regimen of carboplatin/paclitaxel/trastuzumab as one of the recommended therapies for patients with HER2-positive endometrial carcinoma for stage III/IV or recurrent uterine serous carcinoma (category 2A).[9,10]

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POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of trastuzumab products. Approval is recommended for those who meet the Criteria and Dosing for the listed indications. Extended approvals are allowed if the patient continues to meet the **Criteria** and **Dosing**. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with trastuzumab products, as well as the monitoring required for adverse events and long-term efficacy, approval requires trastuzumab products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Herceptin, Hercessi, Herzuma and Ontruzant is recommended for request meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product(s): Kanjinti, Trazimera, Ogivri
Non-Preferred Products(s): Herceptin, Hercessi, Herzuma and Ontruzant

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient meets any *one of the items listed below (A, B, C, D or E)*. *Chart notes documenting* the issue must be provided at time of request:

A. The patient is *not* considered a new start to the non-preferred product (new start is defined as no use of the requested product in the previous 365 days) OR

B. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

C. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

D. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR

E. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered

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- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products.
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

FDA-Approved Indications

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1. Breast Cancer. Approve for the duration noted if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
- **C)** Patient meets ONE of the following (i or ii):
  - **i.** Approve for 1 year (total) if trastuzumab is used for neoadjuvant (preoperative)/adjuvant therapy; OR
  - **ii.** Approve for 1 year if trastuzumab is used for recurrent or metastatic disease; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve ONE of the following dosing regimens (A, B, or C):
- **A)** 4 mg/kg intravenously followed by 2 mg/kg not more frequently than once weekly; OR
- **B)** 8 mg/kg intravenously followed by 6 mg/kg not more frequently than once every 3 weeks; OR
- **C)** 4 mg/kg intravenously followed by 2 mg/kg not more frequently than once weekly during chemotherapy, then 6 mg/kg not more frequently than once every 3 weeks.

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2. Gastric, Esophageal, or Gastroesophageal Junction Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has locally advanced or metastatic disease; AND
- **C)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
- **D)** Patient meets BOTH of the following (i and ii):
  - **i.** Trastuzumab will be used as first-line therapy; AND
  - **ii.** Trastuzumab will be used in combination with chemotherapy; AND
    Note: Examples of chemotherapy are cisplatin, oxaliplatin, capecitabine, 5-fluorouracil (5-FU).
- **E)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
- **A)** 8 mg/kg intravenously followed by 6 mg/kg not more frequently than once every 3 weeks; OR
- **B)** 6 mg/kg intravenously followed by 4 mg/kg not more frequently than once every 2 weeks.

Other Uses with Supportive Evidence

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3. Biliary Tract Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has unresectable or metastatic disease; AND
- **C)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND

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D) The medication will be used in combination with Perjeta (pertuzumab intravenous infusion) or Tukysa (tucatinib tablets); AND
E) The patient has tried one systemic regimen; AND
Note: Examples of a systemic regimen include: gemcitabine and cisplatin, 5-fluorouracil and oxaliplatin, capecitabine and oxaliplatin, or gemcitabine and oxaliplatin.
F) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve 8 mg/kg intravenously followed by 6 mg/kg not more frequently than once every 3 weeks.

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4. Colon or Rectal Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
A) Patient is ≥ 18 years of age; AND
B) Patient has advanced or metastatic disease; AND
C) Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
D) The medication is used in combination with Perjeta (pertuzumab intravenous infusion), lapatinib, or Tukysa (tucatinib tablets); AND
E) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve ONE of the following dosing regimens (A or B):
A) 8 mg/kg intravenously followed by 6 mg/kg not more frequently than once every 3 weeks; OR
B) 4 mg/kg intravenously followed by 2 mg/kg not more frequently than weekly.

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5. Endometrial Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
A) Patient is ≥ 18 years of age; AND
B) Patient has advanced or recurrent uterine serous carcinoma; AND
C) Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
D) Trastuzumab will be used in combination with chemotherapy; AND
Note: Examples of chemotherapy are carboplatin, paclitaxel.
E) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve 8 mg/kg intravenously followed by 6 mg/kg not more frequently than once every 3 weeks.

6. Salivary Gland Tumor. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Patient has recurrent, unresectable, or metastatic disease; AND
C) Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve 8 mg/kg intravenously followed by 6 mg/kg not more frequently than once every 3 weeks.

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CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of trastuzumab is not recommended in the following situations.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Herceptin® intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; February 2021.
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7. The NCCN Head and Neck Cancers Clinical Practice Guidelines in Oncology (version 4.2024 – May 1, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2024.
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10. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 15, 2024. Search term: trastuzumab.
11. Hercessi™ intravenous infusion [prescribing information]. Raleigh, NC: Accord BioPharma; September 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Colon or Rectal Cancer:** Added "Tukysa (tucatinib tablets)" as one of the agents that can be used in combination with trastuzumab.	06/28/2023
Annual Revision	**Biliary Tract Cancer:** Added "Tukysa (tucatinib tablets)" as one of the agents that can be used in combination with trastuzumab.	07/17/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
UCare Update	Moved Ogivri to preferred product status effective 1/1/25. Ogivri will no longer be targeted by the policy.	12/3/2024
Selected Revision	Added Hercessi, a new biosimilar, to the policy.	12/11/2024
UCare Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/07/2025

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