UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – HER2 Antagonist) – Trastuzumab Products Utilization Management Medical Policy

- Herceptin® (trastuzumab intravenous infusion – Genentech)
- Hercessi™ (trastuzumab-strf intravenous infusion – Accord BioPharma)
- Herzuma® (trastuzumab-pkrb intravenous infusion – Celltrion)
- Kanjinti™ (trastuzumab-anns intravenous infusion – Amgen)
- Ogivri® (trastuzumab-dkst intravenous infusion – Mylan)
- Ontruzant® (trastuzumab-dttb intravenous infusion – Merck)
- Trazimera™ (trastuzumab-qyyp intravenous infusion – Pfizer)

REVIEW DATE: 07/16/2025

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 for *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 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 4.2025 – April 17, 2025) 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 4.2025 – June 27, 2025) and NCCN guidelines for rectal cancer (version 2.2025 – March 31, 2025) 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 2.2025 – April 4, 2025) and Esophageal and Esophagogastric Junction Cancers (version 3.2025 – April 22, 2025) 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 4.2025 – June 20, 2025) 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 2.2025 – July 2, 2025) 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 3.2025 – March 7, 2025) 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 or carcinosarcoma (category 2A).[9,10]

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 trastuzumab products is recommended in those who meet one of the following:

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
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.

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; June 2024.
2. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – April 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
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5. The NCCN Gastric Clinical Practice Guidelines in Oncology (version 2.2025 – April 4, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
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7. The NCCN Head and Neck Cancers Clinical Practice Guidelines in Oncology (version 4.2025 – June 20, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
8. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 2.2025– July 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
9. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 3.2025 – March 7, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
10. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025. 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
Selected Revision	Added Hercessi, a new biosimilar, to the policy.	12/11/2024
Update	04/21/2025: The policy name was changed from "Oncology (Injectable) - Trastuzumab Products UM Medical Policy" to "Oncology (Injectable - HER2 Antagonist) - Trastuzumab Products UM Medical Products Policy"	N/A
Annual Revision	No criteria changes	07/16/2025

N/A – Not Applicable.