Trastuzumab Products Clinical Resource

Agents:

- Herceptin® (trastuzumab intravenous infusion – Genentech)
- Herceptin Hylecta (trastuzumab and hyaluronidase-oysk subcutaneous injection- Genentech)
- 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)

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OVERVIEW

Trastuzumab biosimilar products do not require prior authorization; however, the use of BRAND Herceptin requires an evaluation of medical necessity.

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

- **Breast cancer, adjuvant treatment** of HER2 overexpressing node positive or node negative (estrogen receptor/progesterone receptor 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, Ogivri, Ontruzant, Trazimera, and Kanjinti 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.

Herceptin Hylecta subcutaneous injection is a combination of trastuzumab and hyaluronidase, an endoglycosidase which helps with absorption and allows for subcutaneous injection instead of intravenous administration. Herceptin Hylecta is **NOT** interchangeable with any intravenous trastuzumab products and has different dosing and administration instructions. Herceptin Hylecta is approved for breast cancer as above, based on an FDA-approved companion diagnostic for trastuzumab.

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 should be assessed individually on a case-by-case basis. The recommended regimen for trastuzumab and hyaluronidase-oysk is 600 mg/ 10,000 units administered subcutaneously over 2-5 minutes once every three weeks.

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 Tykerb® (lapatinib tablets), trastuzumab is given as a 4 mg/kg infusion on Day 1 of Cycle 1, followed by 2mg/kg weekly.[5-6]

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

Guidelines

Trastuzumab is discussed in guidelines from The National Comprehensive Cancer Network (NCCN)[9]:

- **Breast Cancer:** NCCN guidelines (version 4.2021 – April 28, 2021) recommend trastuzumab in combination with chemotherapy or endocrine therapy for adjuvant treatment of HER2-positive breast cancer (category 1). Trastuzumab in combination with paclitaxel (category 2A) is a preferred preoperative/adjuvant therapy regimen.[2] 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).[2] The guidelines list other trastuzumab-containing regimens for HER2-positive metastatic disease.
- **Colon and Rectal Cancer:** NCCN guidelines for colon cancer (version 2.2021 – January 21 , 2021) and NCCN guidelines for rectal cancer (version 1.2021 – December 22, 2020) list trastuzumab in combination with Perjeta or Tykerb in patients with HER2 amplified disease, RAS and BRAF wild-type disease.[5-6]
- **Gastric Cancer and Esophageal and Esophagogastric Junction Cancers**: NCCN guidelines (version 2.2021 – March 9, 2021) state that for metastatic or locally advanced disease (where local therapy is not indicated) trastuzumab should be added to first-line systemic chemotherapy for HER2-overexpressing adenocarcinoma.[3-4] The recommended regimens for metastatic or locally advanced HER2-positive gastric, esophageal, or esophagogastric junction adenocarcinoma are trastuzumab in combination with cisplatin and a fluoropyrimidine (5-FU or capecitabine) [category 1] or trastuzumab in combination with other chemotherapy agents (category 2B) [various regimens based on individual patient characteristics].[3-4] Trastuzumab is not recommended for use in combination with anthracyclines.
- **Head and Neck Cancers:** NCCN guidelines (version 3.2021- April 27, 2021) 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 pertuzumab or docetaxel (category 2A).[8]
- **Uterine Neoplasms**: NCCN guidelines (version 2.2021– May 7, 2021) list the combination chemotherapy regimen of carboplatin/paclitaxel/trastuzumab as one of the recommended therapies for patients with HER2-positive uterine serous carcinoma (category 2A).[7]

USE OF TRASTUZUMAB

The use of trastuzumab is supported in clinical guidelines in numerous situations and detailed recommendations are available in NCCN. For all indications, prescribing should be in consultation with a specialist in area of expertise (e.g. Oncology, Hematologist, etc.).

FDA-Approved Indications

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1. **Breast Cancer** Use if the patient meets the following criteria):
   - **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 criteria (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

   Dosing: Use 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 (GE) Junction Cancer**. Use if the patient meets the following criteria):
   - **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 the following criteria (i and ii):
     - **i.** Trastuzumab will be used as first-line therapy; AND
     - **ii.** Trastuzumab will be used in combination with chemotherapy Note: Examples of chemotherapy are cisplatin, oxaliplatin, capecitabine, 5-fluorouracil [5-FU].

   Dosing. Use 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. **Colon or Rectal Cancer.** Use if the patient meets the following criteria
   - **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 for injection) or Tykerb (lapatinib tablets)

   Dosing: Use the following dosing regimens (A or B):
   - **A)** 8 mg/kg intravenously followed by 6 mg per/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.

4. **Endometrial Carcinoma. Use** if the patient meets the following criteria
   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;
   Note: Examples of chemotherapy are carboplatin, paclitaxel.

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

5. **Salivary Gland Tumor**. Use if the patient meets the following criteria):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has recurrent, unresectable, or metastatic disease; AND
   Patient has human epidermal growth factor receptor 2 (HER2)-positive disease;
   Dosing: Use8 mg/kg intravenously followed by 6 mg/kg not more frequently than once every 3 weeks.

CONDITIONS NOT RECOMMENDED FOR USE

Use of trastuzumab is not recommended in the following situations.

1. Use is not recommended for circumstances not listed in package labeling or in NCCN. Criteria will be updated as new published data are available.

REFERENCES

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