Trastuzumab Products:

Trastuzumab (Herceptin®), Trastuzumab-anns (Kanjinti®), Trastuzumab-dkst (Ogivri®), Trastuzumab-dttb (Ontruzant®), Trastuzumab-pkrb (Herzuma®), Trastuzumab-qyyp (Trazimera®)

Prior Authorization Drug Coverage Policy

Effective Date: 11/9/2020
Revision Date: n/a
Review Date: 10/4/2021
Lines of Business: Commercial
Policy type: Prior Authorization

This Drug Coverage Policy provides parameters for the coverage of trastuzumab products, which includes Trastuzumab (Herceptin®), Trastuzumab-anns (Kanjinti®), Trastuzumab-dkst (Ogivri®), Trastuzumab-dttb (Ontruzant®), Trastuzumab-pakrb (Herzuma®), and Trastuzumab-qyyp (Trazimera®). Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (NCCN Category 1 or 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1]

The human epidermal growth factor receptor 2 (HER2) proto-oncogene encodes a transmembrane receptor protein of 185 kDa, which is structurally related to the epidermal growth factor receptor. Trastuzumab products have been shown, in both *in vitro* assays and in animals, to inhibit the proliferation of human tumor cells that overexpress HER2.

Trastuzumab products are mediators of antibody-dependent cellular cytotoxicity (ADCC). *In vitro*, trastuzumab product mediated ADCC has been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Trastuzumab is a monoclonal antibody selectively binds to human epidermal growth factor receptor 2 (HER2) proteins thereby inhibiting the proliferation of human tumor cells that over express HER2.

Trastuzumab is available as Herceptin for Injection as single dose 150mg vial. Trastuzumab-anns is available as Kanjinti for injection as 150 mg single dose vial, 420mg multi-dose vial. Trastuzumab-dkst is available as Ogivri for injection as 420mg multi-dose vial or 150 mg single dose vial. Trastuzumab-qyyp is available as Trazimera for injection as 420mg multi-dose vial.

FDA Indications[1]

Trastuzumab (Herceptin®), Trastuzumab-anns (Kanjinti®), Trastuzumab-dkst (Ogivri®), Trastuzumab-dttb (Ontruzant®), Trastuzumab-pkrb (Herzuma®), and Trastuzumab-qyyp (Trazimera®) are FDA indicated for the following:

- The treatment of HER2-positive (3+ by immunohistochemistry) or gene amplification (by fluorescence in situ hybridization) breast cancer.
- The treatment of HER2-positive metastatic gastric or gastroesophageal junction adenocarcinoma.

NCCN Compendium Supported Indications (Herceptin, Kanjinti, Ogivri, Ontruzant, Herzuma, Trazimera)[1-7]

- Breast Cancer
- Central Nervous System Cancers
- Colon Cancer
- Esophageal and Esophagogastric Junction Cancers
- Gastric Cancers
- Rectal Cancer
- Head and Neck Cancers - Salivary Gland Tumors
- Uterine Cancer - Endometrial Carcinoma

Coverage Determinations[1-7]

Trastuzumab (Herceptin®), Trastuzumab-anns (Kanjinti®), Trastuzumab-dkst (Ogivri®), Trastuzumab-dttb (Ontruzant®), Trastuzumab-pkrb (Herzuma®), and Trastuzumab-qyyp (Trazimera®) will require prior authorization. The following agents are considered medically necessary for the following indications if all criteria below are met.

In addition to the below criteria, Trastuzumab-dkst (Ogivri®), Trastuzumab-dttb (Ontruzant®), Trastuzumab-pkrb (Herzuma®) must confirm inadequate response, intolerance, contraindication, or clinical rationale for not using Trastuzumab (Herceptin®), Trastuzumab-anns (Kanjinti®), or Trastuzumab-qyyp (Trazimera®).

Breast Cancer

- The member has a diagnosis of HER2-positive (according to the most recent American Society of Clinical Oncology/College of American Pathologists guidelines) breast cancer **AND**
- One of the following apply:
    - The member will receive neoadjuvant treatment using trastuzumab product for locally advanced breast cancer with one of the NCCN Compendium recommended regimens. (Please refer to the NCCN Compendium for the specific regimens) **OR**
    - The member will receive adjuvant treatment using trastuzumab product for node-positive or node-negative (Estrogen/Progesterone (ER/PR)-negative or with one

high-risk feature) breast cancer with one of the NCCN Compendium recommended regimens (Please refer to the NCCN Compendium for the specific regimens) **OR**

- The member will receive treatment using trastuzumab product for recurrent or metastatic, HR-positive breast cancer with one of the following:
  - In combination with tamoxifen, fulvestrant, or aromatase inhibitor with or without lapatinib **AND**
  - Meets one of the following:
    - Postmenopausal women **OR**
    - Premenopausal women with ovarian ablation/suppression **OR**
    - Males on concomitant suppression of testicular steroidogenesis **OR**
- The member will receive treatment using trastuzumab product for recurrent or metastatic breast cancer that is hormone receptor (HR)-negative or HR-positive with or without endocrine therapy with one of the NCCN Compendium recommended regimens (Please refer to the NCCN Compendium for the specific regimens)

Recommended dosage: 8 mg/kg loading dose followed by 6 mg/kg maintenance dose IV every 3 weeks or 4 mg/kg loading dose followed by 2 mg/kg maintenance IV dose weekly

Central Nervous System Cancers

- The member has a diagnosis of HER2- positive unresectable or metastatic breast cancer with or without brain metastases **AND**
- The member has received ≥1 prior anti-HER2-based regimens in the metastatic setting **AND**
- The member will receive treatment using the trastuzumab product in combination with tucatinib and capecitabine

Recommended dosage: 8 mg/kg loading dose followed by 6 mg/kg maintenance dose IV every 3 weeks

Colorectal Cancer

- The member has a diagnosis of HER2-overexpressing, RAS-wild type advanced or metastatic colorectal cancer **AND**
- The member will receive treatment using trastuzumab product in combination with pertuzumab or lapatanib **AND**
- The member is not appropriate for intensive therapy **AND**
- The member has no previous treatment with a HER2 inhibitor **AND**
- One of the following apply for *primary therapy*:
  - Used as primary treatment for locally unresectable or medically inoperable disease **OR**
  - Used for unresectable synchronous liver or lung metastases or metachronous metastases that remain unresectable after primary systemic therapy **OR**

    - Used as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for patients with existing or imminent obstruction **OR**
    - Used for synchronous unresectable metastases of other sites **OR**
    - Used as primary treatment for unresectable metachronous metastases in patients
        - who have not received previous adjuvant FOLFOX (5-FU/Leucovorin/Oxaliplatin) or Capecitabine/oxaliplatin (CapeOx) within the past 12 months **OR**
        - who have received previous fluorouracil/leucovorin (5-FU/Leucovorin) or capecitabine therapy **OR**
        - who have not received any previous chemotherapy
- One of the following apply for *subsequent therapy* in patients previously treated with:
    - oxaliplatin-based therapy without irinotecan
    - irinotecan-based therapy without oxaliplatin
    - oxaliplatin and irinotecan
    - treatment without irinotecan or oxaliplatin

Recommended dosage: 8 mg/kg loading dose followed by 6 mg/kg maintenance dose IV every 3 weeks or 4 mg/kg loading dose followed by 2 mg/kg maintenance IV dose weekly

Gastric, Esophageal, or Gastroesophageal Junction Adenocarcinoma

- The member has a diagnosis of HER2- positive metastatic gastric or gastroesophageal junction adenocarcinoma **AND**
- The member has not received prior treatment for metastatic disease **AND**
- The member will receive treatment using trastuzumab product
    - in combination with cisplatin and fluorouracil or capecitabine
    - in combination with oxaliplatin and fluorouracil or capecitabine
    - In combination with cisplatin, pembrolizumab and fluorouracil or capecitabine
    - In combination with oxaliplatin, pembrolizumab and fluorouracil or capecitabine

Recommended dosage: 8 mg/kg loading dose followed by 6 mg/kg maintenance dose IV every 3 weeks

Head and Neck Cancers - Salivary Gland Tumors

- The member has a diagnosis of HER2- positive advanced and or recurrent head and neck cancer (salivary gland tumor) **AND**
- The member will receive treatment using trastuzumab
    - as a single agent **OR**
    - in combination with docetaxel **OR**
    - in combination with pertuzumab

Recommended dosage: 8 mg/kg loading dose followed by 6 mg/kg maintenance dose IV every 3 weeks

Uterine Cancer - Endometrial Carcinoma

- The member has a diagnosis of HER2- positive advanced and or recurrent uterine serous carcinoma **AND**
- The member will receive treatment using trastuzumab product in combination with carboplatin and paclitaxel

Recommended dosage: 8 mg/kg loading dose followed by 6 mg/kg maintenance dose IV every 3 weeks

All indications:

- Trastuzumab products will be approved up to a 12-month duration, or as determined through clinical review.

Coverage Limitations

Treatment with a trastuzumab product is not considered medically necessary for members with the following concomitant conditions:

- The member does not have a diagnosis of HER2-overexpressing disease.
- HER2 overexpression is not tested with FDA-approved companion diagnostic.
- The member has cardiac dysfunction that is unsuitable for treatment with trastuzumab product.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary

Contraindications/Warnings/Precautions[1]

- There are no contraindications listed in the US manufacturers' labeling.
- Warnings/Precautions:
    - Exacerbation of Chemotherapy-Induced Neutropenia

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

Description	HCPCS
Inj. trastuzumab, 1 mg	J9355
Inj. trastuzumab-anns, 1 mg	Q5117
Inj. trastuzumab-dkst, 1 mg	Q5114
Inj. trastuzumab-dttb, 1 mg	Q5112
Inj. trastuzumab-pkrb, 1 mg	Q5113
Inj. trastuzumab-qyyp, 1 mg	Q5116

Disclaimer

Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

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