09-J0000-86

Original Effective Date: 02/15/09

Reviewed: 03/12/25

Revised: 04/15/25

Subject: Trastuzumab (Herceptin®, biosimilars) and Trastuzumab and hyaluronidase-oysk (Herceptin Hylecta™) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Trastuzumab (Herceptin) is a monoclonal antibody that antagonizes human epidermal growth factor 2 protein (HER2). Trastuzumab was initially granted US Food and Drug Administration (FDA) approval for the treatment of metastatic breast cancer in September 1998. In 2006, the FDA expanded the approval to include adjuvant treatment of early breast cancer and 2010 first-line treatment of HER2 positive metastatic gastric or gastroesophageal cancer in combination with cisplatin and fluorouracil or capecitabine. In 2019, a subcutaneous formulation of trastuzumab combined with hyaluronidase (Herceptin Hylecta) was approved for the treatment of HER2-overexpressing breast cancer.

HER2 overexpression is seen in 25-30% of breast cancers and 7-34% of gastric cancers; overexpression has been associated with aggressive disease and decreased overall survival.

Trastuzumab is included in National Comprehensive Cancer Network (NCCN) guidelines for treatment of Biliary Tract Cancers (Version 3.2023), Breast Cancer (Version 1.2024), Central Nervous Systems Cancer (Version 1.2023), Colon Cancer (Version 1.2024), Esophageal and Esophagogastric Junction Cancers (Version 4.2019), Gastric Cancer (Version 3.2023), Rectal Cancer (Version 1.2024), and Uterine Neoplasms (Version 5.2019). Trastuzumab in combination with hyaluronidase-oysk is included in NCCN guidelines for treatment of Breast Cancer (Version 2.2020).

Six biosimilar versions of trastuzumab have been FDA approved: Hercessi, Herzuma, Kanjinti, Ogivri, Ontruzant, Trazimera.

POSITION STATEMENT:

Initiation of trastuzumab (Hercessi, Herceptin, Herzuma, Kanjinti, Ogivri, Ontruzant, Trazimera) or trastuzumab in combination with hyaluronidase-oysk (Herceptin Hylecta) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Biliary Tract Cancers: Gallbladder Cancer, Intrahepatic Cholangiocarcinoma, Extrahepatic Cholangiocarcinoma (trastuzumab only)
    a. Member has been diagnosed with unresectable or resected gross residual (R2) disease, or metastatic disease
    b. Member has HER2-positive disease defined as **ONE** of the following:
        i. Immunohistochemistry (IHC) is 3+
        ii. Dual-probe ISH assay results:
            - HER2/CEP17 ratio ≥2.0 AND average HER2 copy number ≥ 4.0 signals/cell
        iii. Concurrent dual-probe ISH assay and IHC results:
            - HER2/CEP17 ratio ≥2.0 AND average HER2 copy number <4.0 signals/cell and concurrent IHC 3+
            - HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥6.0 signals/cell and concurrent IHC 2+ or 3+
            - HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥4.0 and <6.0 signals/cell and concurrent IHC 3+
    c. Trastuzumab will be used in combination pertuzumab (Perjeta)
    d. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brand Herceptin only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to, trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)
    e. Dose does not exceed any of the following:
        i. Initial: 8 mg/kg x 1 dose
        ii. Maintenance: 6 mg/kg every 3 weeks

    Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

2. Breast Cancer (trastuzumab OR trastuzumab in combination with hyaluronidase-oysk)
    a. Member has HER2-positive disease defined as **ONE** of the following:
        i. Immunohistochemistry (IHC) is 3+
        ii. Dual-probe ISH assay results:

- HER2/CEP17 ratio ≥2.0 AND average HER2 copy number ≥ 4.0 signals/cell

iii. Concurrent dual-probe ISH assay and IHC results:

- HER2/CEP17 ratio ≥2.0 AND average HER2 copy number <4.0 signals/cell and concurrent IHC 3+
- HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥6.0 signals/cell and concurrent IHC 2+ or 3+
- HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥4.0 and <6.0 signals/cell and concurrent IHC 3+

b. Use will be for **ANY** of the following:

i. Neoadjuvant therapy

ii. Adjuvant therapy

iii. Metastatic (stage IV) or recurrent disease therapy

iv. Preoperative systemic therapy

c. For brand Herceptin Hylecta only: Use will not be in combination with any intravenous chemotherapy agents

d. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brands Herceptin and Herceptin Hylecta only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to, trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

e. Dose does not exceed:

i. Trastuzumab

- Initial dose: 8 mg/kg x 1 dose
- Maintenance dose: 2 mg/kg weekly **OR** 6 mg/kg every 3 weeks

ii. Trastuzumab in combination with hyaluronidase-oysk

- 600 mg trastuzumab/10,000 units hyaluronidase (1 vial) every 3 weeks

Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

3. Central Nervous System Cancers (trastuzumab only)

a. Member has limited or extensive brain metastases

b. Member has HER2-positive breast cancer defined as ONE of the following:

i. Immunohistochemistry (IHC) is 3+

ii. Dual-probe ISH assay results:

- HER2/CEP17 ratio ≥2.0 AND average HER2 copy number ≥ 4.0 signals/cell

iii. Concurrent dual-probe ISH assay and IHC results:

- HER2/CEP17 ratio ≥2.0 AND average HER2 copy number <4.0 signals/cell and concurrent IHC 3+
- HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥6.0 signals/cell and concurrent IHC 2+ or 3+
- HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥4.0 and <6.0 signals/cell and concurrent IHC 3+

c. Use will be in combination with pertuzumab OR capecitabine and tucatinib (Tukysa)

d. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brand Herceptin only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to, trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

e. Dose does not exceed

i. Initial dose: 8 mg/kg x 1 dose

ii. Maintenance dose: 2 mg/kg weekly OR 6 mg/kg every 3 weeks

Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

4. Colon Cancer (trastuzumab only)

a. Member has HER2-amplified and RAS and BRAF-wildtype disease

b. Trastuzumab will be used in combination with pertuzumab (Perjeta), lapatinib (Tykerb), or tucatinib (Tukysa)

c. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brand Herceptin only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

d. Dose does not exceed **EITHER** of the following:

i. Initial: 8 mg/kg x 1 dose

ii. Maintenance: 6 mg/kg every 3 weeks

Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

5. Rectal Cancer (trastuzumab only)

a. Member has HER2-amplified and RAS and BRAF-wildtype disease

b. Trastuzumab will be used in combination with pertuzumab (Perjeta), lapatinib (Tykerb), or tucatinib (Tukysa)

c. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brand Herceptin only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

d. Dose does not exceed **EITHER** of the following:

   i. Initial: 8 mg/kg x 1 dose

   ii. Maintenance: 6 mg/kg every 3 weeks

   Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

6. Gastric Cancer (trastuzumab only)

   a. Member has HER2 overexpression positive disease

   b. Use will be for palliative therapy or for members with surgically unresectable disease

   c. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brand Herceptin only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

   d. Dose does not exceed:

      i. Initial dose: 8 mg/kg x 1 dose

      ii. Maintenance dose: 6 mg/kg every 3 weeks

      Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

7. Esophageal, or Esophagogastric Junction Adenocarinoma (trastuzumab only)

   a. Member has HER2 overexpression positive disease

   b. Use will be for palliative therapy

   c. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brand Herceptin only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

   d. Dose does not exceed:

      i. Initial dose: 8 mg/kg x 1 dose

      ii. Maintenance dose: 6 mg/kg every 3 weeks

Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

8. Leptomeningeal Metastases (trastuzumab only)
    a. Trastuzumab will be used for intracerebrospinal fluid (CSF) treatment for leptomeningeal metastases from breast cancer
    b. Member has HER2-positive breast cancer disease defined as **ONE** of the following:
        i. Immunohistochemistry (IHC) is 3+
        ii. Dual-probe ISH assay results:
            - HER2/CEP17 ratio ≥2.0 AND average HER2 copy number ≥ 4.0 signals/cell
        iii. Concurrent dual-probe ISH assay and IHC results:
            - HER2/CEP17 ratio ≥2.0 AND average HER2 copy number <4.0 signals/cell and concurrent IHC 3+
            - HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥6.0 signals/cell and concurrent IHC 2+ or 3+
            - HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥4.0 and <6.0 signals/cell and concurrent IHC 3+
    c. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brand Herceptin only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to, trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)
    d. Dose does not exceed:
        i. Initial dose: 8 mg/kg x 1 dose
        ii. Maintenance dose: 2 mg/kg weekly **OR** 6 mg/kg every 3 weeks

    Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

9. Salivary Gland Tumors (trastuzumab only)
    a. Member has HER2-positive disease defined as ONE of the following:
        i. Immunohistochemistry (IHC) is 3+
        ii. Dual-probe ISH assay results:
            - HER2/CEP17 ratio ≥2.0 AND average HER2 copy number ≥ 4.0 signals/cell
        iii. Concurrent dual-probe ISH assay and IHC results:

- HER2/CEP17 ratio ≥2.0 AND average HER2 copy number <4.0 signals/cell and concurrent IHC 3+
- HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥6.0 signals/cell and concurrent IHC 2+ or 3+
- HER2/CEP17 ratio <2.0 AND average HER2 copy number ≥4.0 and <6.0 signals/cell and concurrent IHC 3+

b. Member's disease is recurrent

c. Trastuzumab will be used in combination with pertuzumab (Perjeta)

d. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brands Herceptin and Herceptin Hylecta only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to, trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

e. Dose does not exceed EITHER of the following:

i. Initial: 8 mg/kg x 1 dose

ii. Maintenance: 6 mg/kg every 3 weeks

Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

10. Uterine Neoplasms – Endometrial Carcinoma (trastuzumab only)

a. Trastuzumab will be used for stage III/IV disease in combination with carboplatin and paclitaxel

b. Member has HER2-positive disease defined as **ONE** of the following:

i. Immunohistochemistry (IHC) is 3+

ii. Fluorescent in situ hybridization (FISH) HER2 gene copy is greater than or equal to 6 signals/cell

iii. FISH ratio of HER2 gene/chromosome 17 ratio is greater than or equal to 2.0

c. For trastuzumab-strf (Hercessi), trastuzumab-pkrb (Herzuma), trastuzumab-dttb (Ontruzant), and brands Herceptin and Herceptin Hylecta only: Member has tried and had an inadequate response, contraindication, or intolerable adverse effects to, trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), or trastuzumab-qyyp (Trazimera)

d. Dose does not exceed:

i. Initial dose: 8 mg/kg x 1 dose

ii. Maintenance dose: 2 mg/kg weekly **OR** 6 mg/kg every 3 weeks

Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-

dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

11. Other FDA-approved or NCCN supported diagnosis (not previously listed above; trastuzumab OR trastuzumab in combination with hyaluronidase-oysk)
    a. Member meets one of the following:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    b. Dose does not exceed:
        i. Trastuzumab
            - Initial dose: 8 mg/kg x 1 dose
            - Maintenance dose: 2 mg/kg weekly **OR** 6 mg/kg every 3 weeks
        ii. Trastuzumab in combination with hyaluronidase-oysk
            - 600 mg trastuzumab/10,000 units hyaluronidase (1 vial) every 3 weeks

    Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

Approval duration: 6 months

Continuation of trastuzumab (Hercessi, Herceptin, Herzuma, Kanjinti, Ogivri, Ontruzant, Trazimera) or trastuzumab in combination with hyaluronidase-oysk (Herceptin Hylecta) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of breast cancer, colon cancer (trastuzumab only), rectal cancer (trastuzumab only), gastric, esophageal, or esophagogastric adenocarcinoma (trastuzumab only), leptomeningeal metastases from breast cancer (trastuzumab only), uterine serous carcinoma (trastuzumab only), or other FDA-approved or NCCN supported diagnosis, **OR** the member has previously met all indication-specific initiation criteria
2. If indication for use is adjuvant treatment of breast cancer, member has received fewer than 52 weeks of trastuzumab therapy
3. Dose does not exceed:
    a. Trastuzumab: 2 mg/kg weekly **OR** 6 mg/kg every 3 weeks
    b. Trastuzumab in combination with hyaluronidase-oysk: 600 mg trastuzumab/10,000 units hyaluronidase (1 vial) every 3 weeks

Note: Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed. Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials (MDV). Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed.

Approval duration: 6 months

Trastuzumab meets the definition of medical necessity when used for the following designated Orphan Drug indication (http://www.fda.gov/orphan/designat/list.htm) when the dose does not exceed the maximum FDA-approved dose:

1. Treatment of members with pancreatic cancer that overexpress p185HER2 (i.e., HER-2 positive disease)

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved:

- Trastuzumab: Teatment of HER2 overexpressing breast cancer and metastatic gastric or gastroesophageal junction adenocarcinoma. Trastuzumab should be administered as an intravenous (IV) infusion and should not be administered as an IV push or bolus. The recommended dosage is outlined in Table 1.

Table 1

FDA recommended dosage	
Indication	Dose
Adjuvant HER2-postive breast cancer	**EITHER** of the following 1. Initial dose of 4 mg/kg IV over 90 minutes, followed by 2 mg/kg IV over 30 minutes every week 2. Initial dose of 8 mg/kg IV over 90 minutes, followed by subsequent doses of 6 mg/kg IV over 30 minutes every 3 weeks
Metastatic HER2-positive breast cancer	Initial dose of 4 mg/kg IV over 90 minutes, followed by 2 mg/kg IV over 30 minutes every week
Metastatic HER2-positive Gastric cancer	Initial dose of 8 mg/kg IV over 90 minutes, followed by 6 mg/kg IV over 30-90 minutes every 3 weeks.

- Trastuzumab and hyaluronidase-oysk: Treatment of HER2-overexpressing breast cancer administered as a subcutaneous injection over 2-5 minutes. The recommended dosage is 600 mg/10,000 units (600 mg trastuzumab and 10,000 units hyaluronidase) once every 3 weeks.

Drug Availability:

- Trastuzumab: 150 mg lyophilized powder in a single-dose vial for reconstitution
- Trastuzumab: 420 mg lyophilized powder in a multiple-dose vial for reconstitution
- Trastuzumab and hyaluronidase-oysk: 600 mg trastuzumab and 10,000 units hyaluronidase per 5 mL (120 mg/2,000 units per mL) solution in a single-dose vial

PRECAUTIONS:

BOXED WARNING

- Cardiomyopathy: trastuzumab therapy can result in sub-clinical and clinical cardiac failure manifesting as CHF, and decreased LVEF, with greatest risk when administered concurrently with anthracyclines. Evaluate cardiac function prior to and during treatment. Discontinue trastuzumab for cardiomyopathy.
- Infusion reactions, Pulmonary toxicity: Discontinue trastuzumab for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome.
- Embryo-Fetal Toxicity: Exposure to trastuzumab during pregnancy can result in oligohydramnios, in some cases complicated by pulmonary hypoplasia and neonatal death.

WARNINGS/PRECAUTIONS

Chemotherapy-induced neutropenia: trastuzumab therapy may result in Grade 3-4 neutropenia. Monitor complete blood count.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9355	Trastuzumab, 10 mg
J9356	Injection, trastuzumab, 10 mg and Hyaluronidase-oysk (Herceptin Hylecta)
Q5112	Injection, trastuzumab-pkrb, 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
Q5146	Injection, trastuzumab-strf (Hercessi), biosimilar, 10 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C06.9	Malignant neoplasm of mouth, unspecified

C07	Malignant neoplasm of parotid gland
C08.0 – C08.9	Malignant neoplasm of other and unspecified major salivary glands
C15.3 – C16.9	Malignant neoplasm of esophagus and stomach
C18.0 – C18.9	Malignant neoplasm of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C50.011 – C50.929	Malignant neoplasm of female and male breast
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C78.00-C78.02	Secondary malignant neoplasm of unspecified lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage Products: No National Coverage Determination (NCD) was found at the time of the last guideline revised date. The following Local Coverage Determination (LCD) was reviewed on the last guideline revised date: Trastuzumab (Herceptin), (L34026) located at fcso.com.

DEFINITIONS:

Adjuvant Treatment: Additional cancer treatment given after the primary treatment to lower the risk that the cancer will return. Adjuvant therapy may include chemotherapy, radiation therapy, hormone

therapy, targeted therapy, or biologic therapy. Adjuvant therapy can be used after or in combination with another form of cancer therapy and is commonly used following removal of a cancerous tumor to further help in treatment.

Metastatic cancer: when cancer spreads from the primary site (place where it started) to other places in the body.

Neo-adjuvant treatment: Treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy. It is a type of induction therapy.

RELATED GUIDELINES:

Carboplatin (Paraplatin®) IV, 09-J0000-93
Docetaxel (Taxotere®) IV, 09-J0000-95
Doxorubicin HCl Liposome (Doxil®) IV, 09-J0000-91
Gemcitabine (Gemzar®), 09-J0000-96
Irinotecan HCl Camptosar®) IV, 09-J0000-99
Oxaliplatin (Eloxatin®) IV, 09-J1000-00
Paclitaxel and Paclitaxel (protein-bound) IV, 09-J1000-05
Pertuzumab (Perjeta™) IV, 09-J1000-75

OTHER:

None applicable.

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 2/25/25]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 2/25/25]. Available from: http://clinicaltrials.gov/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2/25/25].
4. Genetech. Herceptin (trastuzumab) injeciton. 2017 [cited 2/25/24]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=492dbdb2-077e-4064-bff3-372d6af0a7a2/.
5. Genetech. Herceptin Hylecta (trastuzumab and hyaluronidase-oysk) injeciton. 2019 [cited 3/28/24]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761106s000lbl.pdf/.
6. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2025 [cited 2/25/25]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
7. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 2/25/25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/12/25.

GUIDELINE UPDATE INFORMATION:

02/15/09	New Medical Coverage Guideline.
04/15/09	Revision; consisting of adding maximum dose and ICD-9 coding.
05/15/09	Revision; consisting of updating ICD-9 coding.
07/15/09	Revision; consisting of updating ICD-9 coding.
10/15/09	Revision; consisting of clarifying dosage, and adding new compendia supported indication and coding update.
04/15/10	Revision; consisting of updating coding.
08/01/10	Revision; consisting of updating coding.
01/15/11	Review and revision; consisting of updating coding, related guidelines and references.
01/15/12	Review and revision to guideline; consisting of updating description, dosage, precautions and reference sections.
04/15/12	Revision to guideline; consisting of adding requirement of HER2 testing for gastric and esophageal cancers.
11/15/12	Review and revision to guideline; consisting of reformatting position statement and modifying coverage criteria, updating precautions, exceptions and references.
04/15/13	Review and revision to guideline; consisting of updating position statement with orphan indications and reformatting. Update references.
04/15/14	Review and revision to guideline; consisting of revising position statement, dosage/administration, precautions/warnings, references, and description section; added definitions; updated program exceptions section.
10/15/14	Revision to guideline; consisting of revising position statement and updating references.
04/15/15	Review and revision to guideline; consisting of description, position statement, coding, references, program exceptions.
10/01/15	Revision consisting of update to Program Exceptions section.
11/01/15	Revision: ICD-9 Codes deleted.
12/15/15	Revision consisting of updating dosing.
04/15/16	Review and revision; description, position statement, coding, references.
04/15/17	Review and revision; description, position statement, dosage/administration, references.
07/15/17	Revision to guideline; updated dosage and administration with new vial size.
12/15/17	Revision to guideline consisting of removing HER2 documentation requirement from position statement.
04/15/18	Review and revision; Updated description, position statement, references.
06/15/18	Revision to guideline; Updated position statement.
08/15/18	Revision to guideline; Updated description, position statement, coding.
05/15/19	Review and revision; Updated description, references.
06/15/19	Revision to guideline; Updated description, position statement, coding to include Herceptin Hylecta.

09/15/19	Revision to guideline; Updated description and position statement to include biosimilars.
10/01/19	Revision: Added HCPCS Q5116 and Q5117, and removed J3590.
02/15/20	Revision to guideline; Updated position statement.
03/15/20	Revision to guideline; Updated position statement.
04/15/20	Review and revision; Updated description, position statement, references.
03/15/21	Revision to guideline; Updated position statement.
10/01/21	Revision to guideline; Updated position statement with preferred biosimilars.
04/15/22	Review and revision; Updated references.
04/15/23	Review and revision; Updated references.
04/15/24	Review and revision; Updated description, position statement, references.
10/01/24	Revision to guideline; Updated position statement.
01/01/25	Revision to guideline; Updated position statement and HCPCS coding.
04/15/25	Review and revision; Updated references.