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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	March 16, 2011
Subject:	Trastuzumab	**Page:**	1 of 6

Last Review Date: March 7, 2025

Trastuzumab

Description

Herceptin (trastuzumab), Hercessi* (trastuzumab-strf), Herzuma (trastuzumab-pkrb), **Kanjinti** (trastuzumab-anns), **Ogivri** (trastuzumab-dkst), **Ontruzant** (trastuzumab-dttb), Trazimera (trastuzumab-qyyp)

Preferred products: Kanjinti, Ogivri, Ontruzant

*This medication is included in this policy but is not available on the market as of yet

Background
Herceptin and its biosimilars are monoclonal antibodies that selectively binds with high affinity to the Human Epidermal Growth Factor Receptor – 2 (HER2) protein. Herceptin and its biosimilars are mediators of antibody-dependent cellular cytotoxicity (ADCC). Herceptin and its biosimilars effects have been shown to be preferentially exerted on HER2-overexpressing cancer cells compared with cancer cells that do not over-express HER2. Hercessi, Herzuma, Kanjinti, Ogivri, Ontruzant, and Trazimera are biosimilars which means that the biological products are approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product (1-7).

Regulatory Status
FDA-approved indications: Herceptin and its biosimilars are indicated: (1-8)

- For the treatment of HER2-overexpressing breast cancer.

- For the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.
- In combination with tucatinib for the treatment of adult patients with RAS wild-type HER2-positive unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy

Herceptin and its biosimilars carry a boxed warning regarding possible risks for cardiomyopathy, infusion reactions, pulmonary toxicity, and embryo-fetal toxicity. Trastuzumab use can result in cardiac failure that manifests as congestive heart failure (CHF) or decreased left ventricular ejection fraction (LVEF), with greatest risk when administered concurrently with anthracyclines (1).

Exposure to Herceptin or its biosimilars during pregnancy can result in oligohydramnios, in some cases complicated by pulmonary hypoplasia and neonatal death. Female patients of reproductive potential should be advised to use effective contraception during treatment and for 7 months following the last dose of Herceptin or its biosimilars (1).

Safety and effectiveness in pediatric patients have not been established (1).

Related policies
Afinitor, Enhertu, Halaven, Herceptin Hylecta, Ibrance, Kadcyla, Margenza, Nerlynx, Perjeta, Phesgo, Tukysa, Tykerb

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Herceptin and its biosimilars may be considered **medically necessary** if the conditions indicated below are met.

Herceptin and its biosimilars may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. HER2-overexpressing breast cancer
    a. HER2 protein overexpression or HER2 gene amplification as determined by an FDA-approved test
2. HER2-overexpressing metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma
    a. HER2 protein overexpression or HER2 gene amplification as determined by an FDA-approved test
3. Unresectable or metastatic colorectal cancer
    a. RAS wild-type, as determined by an FDA-approved test
    b. HER2-positive
    c. Cancer has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy
    d. Used in combination with tucatinib

AND ALL of the following:

a. Prescriber agrees to monitor for cardiac function and pulmonary toxicity
b. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with trastuzumab and for 7 months after the last dose
c. **Non-preferred medications only:** Inadequate treatment response, intolerance, or contraindication to **ONE** of the preferred products (Kanjinti, Ogivri, Ontruzant)

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. HER2-overexpressing breast cancer
2. HER2-overexpressing metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma
3. Unresectable or metastatic colorectal cancer

a. Used in combination with tucatinib

AND ALL of the following:

a. Prescriber agrees to monitor for cardiac function and pulmonary toxicity
b. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Trastuzumab and for 7 months after the last dose

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Herceptin and its biosimilars are monoclonal antibodies that selectively bind with high affinity to the HER2 protein. Herceptin and its biosimilars are mediators of antibody-dependent cellular cytotoxicity (ADCC). Herceptin and its biosimilars effects have been shown to be preferentially exerted on HER2-overexpressing cancer cells compared with cancer cells that do not overexpress HER2 (1-7).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Herceptin and its biosimilars while maintaining optimal therapeutic outcomes.

References

1. Herceptin [package insert]. South San Francisco, CA: Genentech, Inc.; June 2024.
2. Hercessi [package insert]. Raleigh, NC: Accord BioPharma Inc.; April 2024.
3. Herzuma [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; November 2024.
4. Kanjinti [package insert]. Thousand Oaks, CA: Amgen Inc.; December 2024.

5. Ogivri [package insert]. Cambridge, MA: Biocon Biologics Inc.; November 2024.
6. Ontruzant [package insert]. Jersey City, NJ: Organon LLC; June 2021.
7. Trazimera [package insert]. New York, NY: Pfizer Inc.; November 2020.
8. NCCN Drugs & Biologics Compendium® Trastuzumab 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.
9. Tukysa [package insert]. Bothell, WA: Seattle Genetics, Inc.; January 2023.

Policy History

Date	Action
September 2012	Annual editorial and reference update
March 2013	Annual editorial and reference update
June 2013	Editorial and reference update
September 2014	Annual editorial review and reference update
June 2015	Annual editorial and reference update
June 2016	Annual editorial review and reference update Policy number change from 5.04.06 to 5.21.06
June 2017	Annual editorial review
December 2017	Addition of Ogivri
March 2018	Annual Review
December 2018	Addition of biosimilar Herzuma. Changed policy name to Trastuzumab
February 2019	Addition of biosimilar Ontruzant
March 2019	Annual review and reference update. Addition of biosimilar Trazimera
June 2019	Annual review. Addition of biosimilar Kanjinti
December 2019	Annual review. Addition of requirement to trial preferred product
March 2020	Annual review and reference update
June 2020	Annual review
September 2020	Annual review
December 2020	Annual review and reference update. Added Herzuma, Ogivri, Ontruzant, Trazimera as preferred products
April 2021	Clarification added to the t/f, intolerance, C/I to preferred products requirement indicating that it only applies to claims adjudicated through the pharmacy benefit. Added requirement for cardiac and pulmonary toxicity monitoring, HER2 overexpression or gene amplification as confirmed by FDA-approved test, and for females of reproductive potential to be advised to use effective contraception to align with the Herceptin Hylecta criteria
June 2021	Annual review and reference update
June 2022	Annual review and reference update
September 2022	Annual review and reference update

February 2023	Per Tukysa PI update, added indication unresectable or metastatic colorectal cancer
March 2023	Annual review and reference update
June 2023	Annual review and reference update
December 2023	Annual review and reference update. Per FEP, changed preferred products to Kanjinti, Ogivri, and Ontruzant. Also removed Medex requirements. Added t/f requirement of ONE preferred agent to initiation
March 2024	Annual review and reference update
May 2024	Addition of biosimilar Hercessi
June 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.