BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.21.126

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	March 22, 2019
Subject:	Herceptin Hylecta	**Page:**	1 of 4

Last Review Date: March 7, 2025

Herceptin Hylecta

Description

Herceptin Hylecta (trastuzumab and hyaluronidase-oysk)

Background
Herceptin Hylecta contains trastuzumab and hyaluronidase. Trastuzumab has been shown to inhibit the proliferation of human tumor cells that overexpress HER2. In vitro, trastuzumab-mediated antibody-dependent cellular cytotoxicity (ADCC) has been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Hyaluronidase has been shown to increase the absorption rate of a trastuzumab product into the systemic circulation (1).

Regulatory Status
FDA-approved indication: Herceptin Hylecta is a combination of trastuzumab, a HER2/neu receptor antagonist, and hyaluronidase, an endoglycosidase, indicated in adults for: (1)

1. The treatment of HER2-overexpressing breast cancer

Herceptin Hylecta carries a boxed warning regarding possible risks for cardiomyopathy, pulmonary toxicity, and embryo-fetal toxicity. Herceptin Hylecta 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 Hylecta during pregnancy can result in oligohydramnios, in some cases complicated by pulmonary hypoplasia and neonatal death (1).

The safety and effectiveness of Herceptin Hylecta in pediatric patients less than 18 years of age have not been established (1).

Related policies
Enhertu, Kadcyla, Margenza, Nerlynx, Perjeta, Phesgo, Trastuzumab, 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 Hylecta may be considered **medically necessary** if the conditions indicated below are met.

Herceptin Hylecta may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

HER2-overexpressing breast cancer

AND ALL of the following:

1. HER2 protein overexpression or HER2 gene amplification as confirmed by an FDA-approved test
2. Prescriber agrees to monitor for cardiac function and pulmonary toxicity
3. Females of reproductive potential will be advised to use effective contraception during treatment and for 7 months following the last dose
4. 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

Diagnosis

Patient must have the following:

HER2-overexpressing breast cancer

AND ALL of the following:

1. Prescriber agrees to monitor for cardiac function and pulmonary toxicity
2. Females of reproductive potential will be advised to use effective contraception during treatment and for 7 months following 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 Hylecta contains trastuzumab and hyaluronidase. Trastuzumab has been shown to inhibit the proliferation of human tumor cells that overexpress HER2. In vitro, trastuzumab-mediated antibody-dependent cellular cytotoxicity (ADCC) has been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Hyaluronidase has been shown to increase the absorption rate of a trastuzumab product into the systemic circulation. The safety and effectiveness of Herceptin Hylecta in pediatric patients less than 18 years of age have not been established (1).

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

References

1. Herceptin Hylecta [package insert]. South San Francisco, CA: Genentech, Inc.; June 2024.
2. NCCN Drugs & Biologics Compendium® Trastuzumab and hyaluronidase-oysk 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.

Policy History

Date	Action
March 2019	Addition to PA
June 2019	Annual review
December 2019	Annual review. Addition of requirement to trial preferred product
March 2020	Annual review
June 2020	Annual review
September 2020	Annual review
December 2020	Annual review. Revised requirement to trial preferred products to: “Patient must have tried at least two of the preferred products (Herzuma, Kanjinti, Ogivri, Ontruzant, Trazimera) unless the patient has a valid medical exception”
June 2021	Annual review and reference update
June 2022	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
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.