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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	August 3, 2012
Subject:	Perjeta	**Page:**	1 of 6

Last Review Date: March 8, 2024

Perjeta

Description

Perjeta (pertuzumab)

Background

Perjeta (pertuzumab) is indicated for use in combination with trastuzumab and docetaxel in patients with HER2-positive metastatic breast cancer, and for use in combination with trastuzumab and chemotherapy as neoadjuvant or adjuvant therapies in patients with HER2-positive early breast cancer. Perjeta is a recombinant humanized monoclonal antibody which targets the extracellular human epidermal growth factor receptor 2 protein (HER2) dimerization domain. It inhibits HER2 dimerization and blocks HER downstream signaling halting cell growth and initiating apoptosis. Perjeta binds to a different HER2 epitope than trastuzumab so that when used in combination, a more complete inhibition of HER2 signaling occurs (1-3).

Regulatory Status

FDA-approved indications: Perjeta (pertuzumab) is a HER2/neu receptor antagonist indicated for: (1)

1. Use in combination with trastuzumab and docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease
2. Use in combination with trastuzumab and chemotherapy as:
    a. Neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer

b. Adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence

Off-Label Uses: (2-3)

1. Treatment of recurrent disease

Perjeta should be withheld or discontinued if trastuzumab treatment is withheld or discontinued. If docetaxel is discontinued, treatment with Perjeta and trastuzumab may continue (1).

Perjeta carries boxed warnings for left ventricular dysfunction and embryo-fetal toxicity (1).

Perjeta can result in subclinical and clinical cardiac failure manifesting as congestive heart failure (CHF) and decreased left ventricular ejection fraction (LVEF). Perjeta has not been studied in patients with a pretreatment LVEF value of less than 50%, a prior history of CHF, and decreases in LVEF to less than 50%. Assess cardiac function and LVEF prior to initiation of Perjeta and at regular intervals during treatment to ensure that LVEF is within the institution's normal limits (1).

Female patients of reproductive potential should have pregnancy status verified prior to initiation of therapy with Perjeta and advised to use effective contraception during treatment and for 7 months following the last dose of Perjeta in combination with trastuzumab (1).

Perjeta has warnings for infusion-related or hypersensitivity reactions and patients should be monitored for signs and symptoms (1).

The safety and effectiveness of Perjeta in pediatric patients have not been established (1).

Related policies
Afinitor, Enhertu, Herceptin Hylecta, Ibrance, Kadcyla, Margenza, Nerlynx, 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.

Perjeta may be considered **medically necessary** if the conditions indicated below are met.

Perjeta 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. Metastatic or recurrent HER2-positive breast cancer
    a. Used initially in combination with trastuzumab (required) and docetaxel (if tolerated)
    b. **NOT** have a history of prior anti-HER2 therapy or chemotherapy for metastatic disease

2. Neoadjuvant treatment for HER2-positive locally advanced, inflammatory, or early stage breast cancer
    a. Used in combination with trastuzumab and chemotherapy
    b. Greater than 2 cm in diameter **OR** node positive

3. Adjuvant therapy for HER2-positive early stage breast cancer
    a. Used in combination with trastuzumab and chemotherapy

AND ALL of the following:

a. Females of childbearing potential should have pregnancy excluded before the start of treatment with Perjeta, prevented during therapy and for 7 months after treatment cessation
b. Left ventricular ejection fraction (LVEF) is above 50%

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Metastatic or recurrent HER2-positive breast cancer

AND ALL of the following:

a. Used in combination with trastuzumab (required) and docetaxel (if tolerated)
b. Left ventricular ejection fraction (LVEF) is above 50%

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Perjeta (pertuzumab) is indicated for use in combination with trastuzumab and docetaxel in patients with HER2-positive metastatic breast cancer, and for use in combination with trastuzumab and chemotherapy as neoadjuvant or adjuvant therapies in patients with HER2-positive early breast cancer. Perjeta carries boxed warnings for left ventricular dysfunction, and embryo-fetal toxicity. Perjeta has warnings for infusion-related reactions and hypersensitivity reactions/anaphylaxis. The safety and effectiveness of Perjeta in pediatric patients have not been established (1-3).

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

References

1. Perjeta [package insert]. South San Francisco, CA: Genentech, Inc.; February 2021.
2. NCCN Drugs & Biologics Compendium® Pertuzumab 2024. National Comprehensive Cancer Network, Inc. Accessed on January 11, 2024.
3. NCCN Clinical Practice Guidelines in Oncology® Breast Cancer (Version 5.2023). National Comprehensive Cancer Network, Inc. December 2023. Accessed on January 11, 2024.

Policy History

Date	Action
July 2012	New Addition
September 2012	Annual editorial and reference update
March 2013	Annual editorial and reference update
June 2013	Editorial review and reference update
October 2013	Addition of new FDA indication of neoadjuvant therapy for the treatment of HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a combined therapy with trastuzumab and docetaxel
September 2014	Annual editorial and reference update
June 2015	Annual editorial review and reference update
June 2016	Annual editorial review and reference update Policy number change from 5.04.20 to 5.21.20
July 2017	Annual editorial review and reference update
January 2018	Addition of new indication: adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence and recurrent HER2-positive breast cancer Removal of the requirement “not to have a history of prior anti-HER2 therapy or chemotherapy for metastatic disease. (Prior anti-HER2 therapy as adjuvant or neoadjuvant therapy is acceptable.)” Removal of the quantity requirement Addition of the requirement for females of childbearing potential should have pregnancy excluded before the start of treatment with Perjeta, prevented during therapy and for 7 months after treatment cessation and addition of left ventricular ejection fraction (LVEF) is above 50%
March 2018	Annual review
June 2019	Annual review and reference update
December 2019	Annual review
March 2020	Annual review and reference update
June 2020	Annual review
September 2020	Annual review
December 2020	Annual review
June 2021	Annual editorial review and reference update
September 2022	Annual review and reference update
June 2023	Annual review and reference update

March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.