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<th>Prescription Drugs</th>
<th><strong>Effective Date:</strong></th>
<th>July 1, 2016</th>
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<td><strong>Subsection:</strong></td>
<td>Antineoplastic Agents</td>
<td><strong>Original Policy Date:</strong></td>
<td>August 3, 2012</td>
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**Last Review Date:** June 24, 2016

### Perjeta

#### Description

**Perjeta (pertuzumab)**

#### Background

Perjeta (pertuzumab) is approved for use in combination with Herceptin (trastuzumab) and docetaxel in people with HER2-positive breast cancer that has spread to different parts of the body (metastatic) and who have not received anti-HER2 therapy or chemotherapy for metastatic breast cancer. Perjeta is also approved for use prior to surgery in combination with Herceptin and docetaxel in people with HER2-positive, locally advanced, inflammatory, or early stage (tumor is greater than 2 cm in diameter or node positive) breast cancer (1).

#### Regulatory Status

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

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. Used in combination with trastuzumab and docetaxel as 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.

#### Limitations of Use:
The safety of Perjeta as part of a doxorubicin-containing regimen has not been established. The safety of Perjeta administered for greater than 6 cycles for early breast cancer has not been established (1).

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 a boxed warning for embryo-fetal toxicity when administered to a pregnant woman. Perjeta carries a pregnancy category D status based on treatment studies done on pregnant cynomolus monkeys with pertuzumab, which resulted in oligohydramnios, delayed fetal kidney development, and embryo-fetal death. It is important to verify pregnancy status prior to the initiation of Perjeta and to advise patients of the risks of embryo-fetal death and birth defects (1).

Pertuzumab has a boxed warning regarding cardiomyopathy. Perjeta can result in subclinical and clinical cardiac failure manifesting as congestive heart failure (CHF), and decreased left ventricular ejection fraction (LVEF). 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).

Pertuzumab may cause infusion-related or hypersensitivity reactions and should be monitored for signs and symptoms (1).

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

Related policies
Kadcyla, Herceptin, Ibrance, 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 for patients 18 years of age or older for the treatment of HER2 overexpressing metastatic breast cancers as part of a combined therapy with trastuzumab and docetaxel. Perjeta may be considered medically necessary for 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.
Perjeta is considered investigational in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age
18 years of age or older

Diagnoses

Patient must have the following:

HER2-positive breast cancer

AND ONE of the following:

1. Metastatic
   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. (Prior anti-HER2 therapy as adjuvant or neoadjuvant therapy is acceptable.)

2. Locally advanced, inflammatory, or early stage
   a. Used in combination with trastuzumab and docetaxel (if tolerated) as neoadjuvant treatment
   b. Greater than 2 cm in diameter OR node positive

Prior – Approval Renewal Requirements

Age
18 years of age or older

Diagnosis

Patient must have the following:
HER2-positive breast cancer

**AND ONE** of the following:
1. Metastatic
   a. Used in combination with trastuzumab (required) and docetaxel (if tolerated)

### Policy Guidelines

**Pre – PA Allowance**
None

**Prior - Approval Limits**

| Quantity | Locally advanced, inflammatory, or early stage breast cancer: 7 vials (6 cycles)  
Metastatic breast cancer: No quantity limit |
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<td>Duration</td>
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**Prior – Approval Renewal Limits**

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### Rationale

**Summary**

Perjeta (pertuzumab) is approved for the treatment of Human Epidermal Growth Factor Receptor-2 (HER2)-positive metastatic, locally advanced, inflammatory, or early stage breast cancers. Perjeta is indicated to be used in conjunction with Herceptin (trastuzumab), another anti-HER2 therapy, and docetaxel. If docetaxel therapy is discontinued, Perjeta and trastuzumab therapy may be continued. If trastuzumab is withheld or discontinued, Perjeta should be withheld or discontinued. Pertuzumab use can result in decreased left ventricular ejection fraction (LVEF). Perjeta carries a boxed warning for embryo-fetal toxicity when administered to a pregnant woman (1).

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

Policy History

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<tr>
<td>July 2012</td>
<td>New Addition</td>
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<tr>
<td>September 2012</td>
<td>Annual editorial and reference update</td>
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<td>March 2013</td>
<td>Annual editorial and reference update</td>
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<tr>
<td>June 2013</td>
<td>Editorial review and reference update</td>
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<tr>
<td>October 2013</td>
<td>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</td>
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<tr>
<td>September 2014</td>
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<tr>
<td>June 2016</td>
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<td>Policy number change from 5.04.20 to 5.21.20</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 24, 2016 and is effective on July 1, 2016.

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