I. PURPOSE

To define and describe the accepted indications for Perjeta (pertuzumab) usage in the treatment of cancer.

II. DEFINITIONS

**Perjeta (pertuzumab):** A recombinant DNA-derived humanized monoclonal antibody, binds to the extracellular dimerization domain of the human epidermal growth factor receptor 2 (HER2) protein. By binding to the HER2 protein, pertuzumab inhibits the growth of tumor cells and mediates antibody-dependent cellular cytotoxicity (ADCC) in cancer cells that overexpress the HER2 protein.

Perjeta (pertuzumab) is FDA approved for the following indications: 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) In combination with trastuzumab and chemotherapy 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, and 3) In combination with trastuzumab and chemotherapy as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.

Perjeta (pertuzumab) is available in Intravenous solution: 420 mg/14 mL single use vial.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

**Inclusion Criteria:** Perjeta (pertuzumab) may be considered medically necessary when any of the following selection criteria is met:

1. **Breast Cancer**
   a. Perjeta (pertuzumab) is being used in members with ALL of the following:
      i. HER-2 overexpression defined as IHC 3+ or FISH amplification ratio ≥ 2 AND
      ii. ECOG performance status of 0-1 AND
iii. A baseline left ventricular ejection fraction (LVEF) of 50% or greater **AND**

iv. For recurrent or metastatic breast cancer in combination with trastuzumab and docetaxel (or paclitaxel) as first line therapy **OR**

v. For recurrent or metastatic breast cancer in combination with trastuzumab with or without cytotoxic therapy (e.g., Vinorelbine or taxane) as second line if previously treated with trastuzumab and chemotherapy **AND** is pertuzumab naive **OR**

vi. For locally advanced, inflammatory, or early stage breast cancer (greater than 2cm or node positive) for the following neoadjuvant or adjuvant treatments (if a pertuzumab-containing regimen was not used as neoadjuvant therapy):

   a. In combination trastuzumab and paclitaxel or docetaxel following AC (doxorubicin and cyclophosphamide) regimen

   b. In combination with TCH (docetaxel, carboplatin, and trastuzumab) regimen

**Exclusion Criteria:** Perjeta (pertuzumab) is not considered medically necessary when any of the following selection criteria is met:

1. The member has HER-2 negative disease.

2. The member has ECOG performance status 2 or greater **OR** a baseline LVEF of < 50%.

3. Dosing exceeds single dose limit of Perjeta (pertuzumab) 840 mg (initial dose) or 420 mg (subsequent dose) every 3 weeks.

4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

**IV. PROCEDURE**

Requests for Perjeta (pertuzumab) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration**

   a. 840 mg IV infusion over 60 minutes, plus trastuzumab 8 mg/kg IV infusion over 90 minutes, plus docetaxel 75 mg/m². Then every 3 weeks, the recommended maintenance dose is pertuzumab 420 mg IV infusion over 30 to 60 minutes, plus trastuzumab 6 mg/kg IV infusion over 30 to 90 minutes, plus docetaxel 100 mg/m² if initial docetaxel dose is tolerated. Dose reductions of pertuzumab are not recommended.

2. **Dosage Adjustments:** Dosage adjustments are not required for renal or hepatic impairment.

3. **Monitoring**

   a. Assess human epidermal growth factor receptor 2 (HER2) status, using a laboratory with demonstrated proficiency in the specific technology being utilized, to determine HER2 overexpression as a requirement for therapy. Patients with evidence of HER2 overexpression defined as 3+ IHC by Dako Herceptest (TM) or FISH amplification ratio 2 by Dako HER2 FISH PharmDx (TM) test kit were included in the clinical trial.
b. Verify negative pregnancy status before initiating therapy. Exposure to pertuzumab can result in embryo-fetal death and birth defects. Advise patients of these risks and the need for effective contraception.

c. Assess left ventricular ejection fraction before initiating therapy and periodically (eg, every 3 months) throughout therapy.
   1. LVEF of less than 40%, or LVEF 40% to 45% with a 10% or greater absolute decrease below pretreatment values: withhold Perjeta (pertuzumab) and Herceptin (trastuzumab) dosing for at least 3 weeks; resume if the LVEF is greater than 45% or is 40% to 45% with less than a 10% absolute decrease below pretreatment values.
   2. If LVEF has not improved within approximately 3 weeks or has deteriorated further, discontinuation of Perjeta (pertuzumab) and Herceptin (trastuzumab) should be strongly considered unless benefits outweighs risks.

d. Observe patients for 60 minutes after the first infusion and 30 minutes after subsequent infusions for infusion-associated reactions and hypersensitivity reaction/anaphylaxis.

e. Monitor patients who become pregnant during therapy for oligohydramnios.

V. APPROVAL AUTHORITY
   1. Review – UM Department
   2. Final Approval – UM Committee

VI. ATTACHMENTS

VII. REFERENCES
   5. Genentech USA, Inc. South San Francisco, 2019.