Approved: Do Not Implement Until 4/30/19

Trastuzumab-pkrb

NDC CODE(S) 63459-0305-xx Herzuma 420 mg/vial (Teva Pharmaceuticals USA)

DESCRIPTION

Trastuzumab-pkrb is a humanized IgG1 kappa monoclonal antibody that selectively binds with high affinity to the extracellular domain of the human epidermal growth factor receptor 2 protein, HER2. Trastuzumab-pkrb is produced by recombinant DNA technology in a mammalian cell (Chinese Hamster Ovary) culture.

Trastuzumab-pkrb is biosimilar to trastuzumab and is likewise a mediator of antibody-dependent cellular toxicity (ADCC). As with trastuzumab, its product-mediated ADCC is preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2.

POLICY

- Trastuzumab-pkrb for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Breast cancer
  - Central Nervous system cancers
  - Endometrial carcinoma
  - Esophageal cancer
  - Esophagogastric junction adenocarcinoma
  - Gastric cancer
- Trastuzumab-pkrb for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Trastuzumab-pkrb is considered **medically appropriate** if **ALL** of the following:
  - Baseline left ventricular ejection fraction (LVEF) is within normal limits
  - Individual is 18 years of age or older
  - Cancer is human epidermal growth factor receptor 2 (HER2)-positive
  - Diagnosis of **ANY ONE** of the following:
    - Breast cancer, invasive, if **ANY ONE** of the following:
      - Preoperative systemic therapy for breast conservation
      - Adjuvant systemic therapy
      - Recurrent or metastatic disease
    - Central nervous system cancer if **ALL** of the following:
      - Individual has leptomeningeal metastases from HER2-positive breast cancer
      - Treatment will be administered intrathecally
    - Endometrial carcinoma if **ALL** of the following:
      - Disease is advanced or recurrent uterine serous carcinoma
      - Used in combination with carboplatin and paclitaxel
    - Gastric, esophageal or esophagogastric junction cancers if **ALL** of the following:
      - Disease is metastatic or locally advanced
      - Used in combination therapy with cisplatin and fluorouracil (5FU) for first-line therapy

Human Epidermal Growth Factor Receptor 2 Protein, HER2 Overexpression Criteria by ANY ONE of the following:

- Immunohistochemistry (IHC) assay 3+
- Fluorescence in situ hybridization (FISH) assay ≥2.0 (HER2/CEP17 ratio)
- Average HER2 copy number ≥ 6 signals/cell

RENEWAL CRITERIA

- Trastuzumab-pkrb is considered **medically appropriate** if for renewal if **All** of the following:
  - Individual continues to meet **ALL** of the initial criteria
  - Tumor shows response with stabilization of disease or decrease in size of tumor or tumor spread
  - Absence of unacceptable toxicity from the drug, e.g., cardiotoxicity, such as left ventricular dysfunction or cardiomyopathy; pulmonary toxicity (e.g., pneumonitis); neutropenia; neurotoxicity; infusion-related and hypersensitivity reactions
  - Left ventricular ejection fraction (LVEF) has not had an absolute decrease of more than 15% from baseline and is within normal limits

INDICATION(S)	DOSAGE & ADMINISTRATION
Breast cancer, Endometrial, Gastric, Esophageal and Esophagogastric Junction Cancers	**Loading dose**: 8mg/kg x 1 for every 21 days dosing schedule Maintenance dose: 6mg/kg every 21 days OR **Loading dose**: 4mg/kg x 1 for weekly (7 days) dosing schedule Maintenance dose: 2mg/kg every 7 days
Leptomeningeal Metastases from Breast Cancer	Escalating doses up to 100 mg intrathecally weekly. - Dosing is highly variable and should be individualized.

LENGTH OF AUTHORIZATION

Coverage will be provided for six months and may be renewed

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice

Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

BlueCross BlueShield Association. Medical Policy Reference Manual. (7:2017). *Trastuzumab* (5.01.12). Retrieved December 31, 2018 from BlueWeb.

Lexi-Comp Online. (2018). AHFS DI. *Trastuzumab.* Retrieved December 31, 2018 from Lexi-Comp Online with AHFS.

MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2018, December). *Trastuzumab.* Retrieved December 31, 2018 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2018). NCCN Drugs & Biologics Compendium®. *Trastuzumab*. Retrieved December 31, 2018 from the National Comprehensive Cancer Network.

U.S. Food and Drug Administration. (2018, December). Center for Drug Evaluation and Research. *Herzuma® (trastuzumab-pkrb) for injection*. Retrieved December 31, 2018 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761091s000lbl.pdf.

EFFECTIVE DATE 4/30/2019

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