Draft Revised Policy: Do Not Implement

Trastuzumab-dttb

DESCRIPTION

Trastuzumab is a recombinant DNA-derived IgG1 kappa monoclonal antibody that selectively binds to the extracellular domain of the human epidermal growth factor receptor 2 protein, HER2. Trastuzumab has been shown to inhibit the proliferation of human tumor cells that overexpress HER2. Trastuzumab is also a mediator of antibody-dependent cellular cytotoxicity (ADCC). Trastuzumab-mediated ADCC, a method of cancer cell destruction, is preferentially exerted on those cancer cells which overexpress HER2.

Trastuzumab-dttb is biosimilar to trastuzumab. Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity has been demonstrated for the conditions of use in indications, dosing regimens, strengths, dosage forms and routes of administration.

POLICY

- Trastuzumab 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
  - Esophageal cancer
  - Esophagogastric junction adenocarcinoma
  - Gastric cancer
  - Uterine cancer
- Trastuzumab for the treatment of other conditions/diseases is considered ***investigational.***

See also: Trastuzumab, Trastuzumab-pkrb, Trastuzumab-qyyp

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Trastuzumab-dttb 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:
    - Invasive breast cancer that is HER2-over-expressing* if used as **ANY ONE** of the following:
      - Adjuvant therapy if **ANY ONE** of the following:
        - In combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.)
        - As a single agent following anthracycline-based therapy
      - Neoadjuvant therapy for breast preservation in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.)
      - Treatment of recurrent or metastatic disease as **ANY ONE** of the following:
        - Single agent in individuals who have received one or more prior treatments for metastatic disease
        - First-line therapy in combination with paclitaxel
        - In combination with endocrine~~, cytotoxic, or lapatinib~~ therapy with hormone receptor-positive or asymptomatic visceral disease if individual is **ANY ONE** of the following:

        - Post-menopausal
        - Pre-menopausal treated with ovarian ablation/suppression if prior endocrine therapy within 1 year **OR** no prior endocrine therapy within 1 year
        - Male receiving concomitant suppression of testicular steroidogenesis
    - Disease is hormone receptor-negative OR hormone receptor-positive refractory to endocrine therapy OR symptomatic visceral disease OR visceral crisis and used in combination with **ANY ONE** of the following:
        - Cytotoxic chemotherapy
        - Lapatinib
        - Pertuzumab and a taxane as first-line therapy
        - Pertuzumab as second-line therapy in patients who were previously treated with trastuzumab without pertuzumab
    - ~~In combination with pertuzumab as second-line therapy if **ALL** of the following:~~
        - ~~Previously treated with trastuzumab and chemotherapy~~
        - ~~Not previously treated with pertuzumab~~
- Central nervous system cancer if **ALL** of the following:
    - Individual has leptomeningeal metastases from HER2-positive breast cancer
    - Treatment will be administered intrathecally
- Gastric, esophageal or esophagogastric junction cancers that is HER2-overexpressing* if **ALL** of the following:
    - Disease is metastatic or locally advanced adenocarcinoma
    - Used in combination therapy with cisplatin and fluorouracil (5FU) or capecitabine for first-line therapy
- Uterine cancer if **ALL** of the following:
    - Used in combination with carboplatin and paclitaxel
    - Used for advanced or recurrent uterine serous carcinoma

***HER2-positive overexpression criteria confirmed by ANY ONE of the following NCCN-defined methods:**
• Immunohistochemistry (IHC) assay 3+ • In situ hybridization (ISH) assay average HER2 copy number ≥ 6.0 signals/cell • Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2

RENEWAL CRITERIA

- Trastuzumab-dttb 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
    - Use for neoadjuvant and adjuvant breast cancer treatment is limited to a total of 52 weeks of therapy

INDICATION(S)	DOSAGE & ADMINISTRATION
Breast cancer	**Loading dose**: 8mg/kg x 1 for every 21 days dosing schedule

Gastric, Esophageal and Esophagogastric Junction Cancers	**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.
Uterine Cancer	**Loading dose:** 8 mg/kg x 1 for every 21 days dosing schedule **Maintenance dose**: 6 mg/kg every 21 days

LENGTH OF AUTHORIZATION

Coverage will be provided for six months and may be renewed;
Use in the neo-adjuvant and adjuvant setting is limited to a total of 52 weeks of treatment

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

Lexi-Comp Online. (2019, February). AHFS DI. *Trastuzumab.* Retrieved March 28, 2019 from Lexi-Comp Online with AHFS.

MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2019, March). *Trastuzumab.* Retrieved March 28, 2019 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2019). NCCN Clinical Practice Guidelines Version 3.2018®. *Invasive breast cancer*. Retrieved March 28. 2019 from the National Comprehensive Cancer Network.

This document has been classified as public information

U.S. Food and Drug Administration. (2019, January). Center for Drug Evaluation and Research. *Ontruzant® (trastuzumab-dttb) for injection, for intravenous use*. Retrieved February 4, 2019 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761100s000lbl.pdf.

EFFECTIVE DATE

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