Draft Revised Policy: Do Not Implement

Pertuzumab (Perjeta®)

DESCRIPTION

Pertuzumab is a recombinant monoclonal antibody. It is an antineoplastic agent that targets the human epidermal growth factor receptor 2 protein known as HER2. It blocks two major intracellular signaling pathways, mitogen-activated protein (MAP) kinase and phosphoinositide 3-kinase (PI3K). This results in cell growth arrest and apoptosis (cell destruction), inhibiting the proliferation of human tumor cells. By combining pertuzumab with trastuzumab, tumor inhibition was significantly increased.

POLICY

- Pertuzumab for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Breast Cancer
  - Colorectal Cancer
  - Head and Neck Cancer ~~Tumors~~
- Pertuzumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Therapy will not be used in combination with pertuzumab/trastuzumab and hyaluronidase-zzxf (Phesgo); **AND**

Breast Cancer

- Used as neoadjuvant (or preoperative) or adjuvant treatment; **AND**
  - Patient has locally advanced, ~~or~~ node positive, or inflammatory disease; **AND**
  - Used in combination with a trastuzumab-based regimen; **OR**
- Used for recurrent unresectable or metastatic disease OR inflammatory breast cancer with no response to preoperative systemic therapy; **AND**
  - Used as first-line therapy in combination with trastuzumab and either paclitaxel **OR** docetaxel; **OR**
  - Used as subsequent therapy in combination with a trastuzumab-based regimen; **AND**
    - Patient was previously treated with trastuzumab and chemotherapy; **AND**
    - Patient has not previously received pertuzumab

Colorectal Cancer

- Used for RAS and BRAF wild-type (WT) disease in combination with trastuzumab; **AND**
- Patient has ~~in patients who have~~ not previously received HER2-targeted therapy; **AND**
  - Used as subsequent therapy for progression of advanced or metastatic disease after at least one prior line of treatment in the advanced or metastatic disease setting; **OR**

- Patient is not appropriate for intensive therapy; **AND**
  - Used as primary treatment for unresectable (or medically inoperable), locally advanced or metastatic disease (*excluding use as neoadjuvant therapy* ~~in rectal cancer~~); **OR**
  - Used for unresectable (or medically inoperable) metastatic disease ~~metastases~~ that remains unresectable after primary systemic therapy

Head and Neck Cancer ~~Tumors~~

- Patient has ~~Used for~~ salivary gland tumors; **AND**
- Used in combination with trastuzumab; **AND**
- Used for one of the following:
  - Recurrent disease with distant metastases; **OR**
  - Unresectable locoregional recurrence with prior radiation therapy (RT); **OR**
  - Unresectable second primary with prior RT

***HER2-positive overexpression criteria ~~of ANY ONE of the following:~~**

• Immunohistochemistry (IHC) assay 3+; OR
• Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number ≥ 4.0 signals/cell; OR
• Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one ~~**ANY ONE**~~ of the following:
  ○ HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; OR
  ○ HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; OR
  ○ HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+

❖*If confirmed using an immunotherapy assay - http://www.fda.gov/companiondiagnostics*

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified Initial Approval Criteria; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: left ventricular dysfunction, severe infusion-related reactions, hypersensitivity reactions/anaphylaxis, etc.; **AND**
- Left ventricular ejection fraction (LVEF) within the previous 3 months as follows:
  - Neoadjuvant and adjuvant breast cancer: LVEF is ≥ 50% OR LVEF has had an absolute decrease of < 10% from baseline
  - All other indications: LVEF is >45% OR LVEF is ≥40% to 45% and absolute decrease is <10% from baseline (~~LVEF results must be within the previous 3 months~~); **AND**
- Use for neoadjuvant and adjuvant breast cancer treatment is limited to a total of 1 year of treatment (total of 18 cycles)

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Breast Cancer	Administer 840 mg intravenously x 1 dose, then 420 mg intravenously every 21 days thereafter until disease progression or unmanageable toxicity • Neoadjuvant therapy consists of 3 to 6 cycles prior to surgery

	• Use for neoadjuvant and adjuvant early breast cancer treatment is limited to a total of 1 year of treatment (total of 18 cycles) **Note: When used for metastatic breast cancer, therapy may be continued until disease progression or unmanageable toxicity.*
Colorectal Cancer	Administer 840 mg intravenously x 1 dose, then 420 mg intravenously every 21 days thereafter until disease progression or unmanageable toxicity
Head & Neck Cancer ~~Tumors~~	Administer 840 mg intravenously x 1 dose, then 420 mg intravenously every 21 days thereafter until disease progression or unmanageable toxicity.

LENGTH OF AUTHORIZATION

- Coverage is provided for 6 months and may be renewed (unless otherwise specified).
- Use for neo-adjuvant and adjuvant breast cancer is limited to a total of 1 year of treatment [18 cycles] *(*Note: When used for recurrent or metastatic breast cancer, therapy may be continued until disease progression or unmanageable toxicity.)*

DOSAGE LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

Loading Dose

- 840 billable units x 1 dose

Maintenance Dose

- 420 billable units every 21 days

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

1. Perjeta [package insert]. South San Francisco, CA; Genentech, Inc.; February 2021 Accessed July 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pertuzumab. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2021.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 6.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2021.
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10. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer 2.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
11. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer 1.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2021.
12. Meric-Bernstam F, Hurwitz H, Raghav KPS, et al. Pertuzumab plus trastuzumab for HER2- amplified metastatic colorectal cancer (My Pathway): an updated report from a multicentre, open-label, phase 2a, multiple basket study. Lancet Oncol. 2019;20(4):518-530. doi:10.1016/S1470-2045(18)30904-5.
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14. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Head and Neck Cancer 1.2021. National Comprehensive Cancer Network, 2021. NATIONAL

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EFFECTIVE DATE

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