Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 04/11/2024

Trastuzumab Class Policy

Herceptin® (trastuzumab)
Herzuma® (trastuzumab-pkrb)
Kanjinti™ (trastuzumab-anns)
Ogivri™ (traztuzumab-dkts)
Ontruzant® (trastuzumab-dttb)
Trazimera™ (trastuzumab-qyyp)

HCPCS: Herceptin: J9355; Herzuma: Q5113; Kanjinti: Q5117; Ogivri: Q5114; Ontruzant: Q5112; Trazimera: Q5116

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Must have human epidermal growth factor receptor 2 (HER2) positive breast cancer, metastatic gastric cancer, gastroesophageal junction adenocarcinoma, or colorectal cancer defined as in situ hybridization (ISH) positive by any of the following:
      i. Single probe average HER2 copy number greater than or equal to 6.0 signals/cell
      OR
      ii. Dual-probe HER2/CEP17 ratio greater than or equal to 2.0
      OR
      iii. Dual-probe HER2/CEP17 ratio less than 2.0 with an average HER2 copy number greater than or equal to 6.0 signals/cell
   b. Must be used with concomitant treatment according to FDA indication or NCCN category 1 or 2A recommendation
   c. Coverage will be provided for biosimilar products for FDA labeled indications of the innovator product when criteria are met
   d. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time

c. Renewal Criteria:
    i. When used as adjuvant breast cancer treatment: Treatment continued until unacceptable toxicity or disease progression for up to a total of 52 weeks of therapy
    ii. For metastatic breast cancer, colorectal cancer, or gastric or gasetoesophageal junction cancer: Treatment continued until unacceptable toxicity or disease progression

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Herceptin and its biosimilars are anti-HER2 monoclonal antibodies that bind to the HER2 receptor and inhibit proliferation of tumor cells that overexpress the receptor. Both breast and gastric cancers can be positive for the HER2 receptor. Herceptin and the trastuzumab biosimilars have been studied in these tumor types and are guideline recommended for use. When used as adjuvant therapy, trastuzumab should be given for a total of 52 weeks of therapy. When used in metastatic disease, treatment should continue indefinitely until unacceptable toxicity or disease progression. Trastuzmab products are not effective against tumors that do not overexpress the HER2 receptor.

- The National Comprehensive Cancer Network (NCCN) 2024 Breast Cancer guidelines and NCCN 2024 Gastric Cancer guidelines support the use of the American Society of Clinical Oncology (ASCO)/College of American Pathologist (CAP) HER2 testing guidelines. The guidelines define tumors as HER2-positive when they meet any of the following: a single probe average HER2 copy number greater than or equal to 6.0 signals/cell, a dual-probe HER2/CEP17 ratio greater than or equal to 2.0, or a dual-probe HER2/CEP17 ratio less than 2.0 with an average HER2 copy number greater than or equal to 6.0 signals/cell.

- NCCN guidelines category 1 recommendations are based on high levels of evidence and uniform concensus that the recommendation is appropriate. Category 2A recommenations are based on a lower level of evidence but still have NCCN uniform concensus the recommenations are appropriate. Category 2B and lower recommendtions are based on low levels of evidence and do no have concensus the recommendation is appropriate, therefore, these treatment regimens should only be used when all other options have been exhausted.

- Where guidelines recommend trastuzumab to be used in combination with other agents as part of a treatment regimen it should be administered as such. Studies have been completed to support use as combination therapy in these scenarios. There are situations where use as a single agent is warranted, for instance, in breast cancer following multiple modality anthracycline therapy. When recommended, trastuzumab can be given as monotherapy.

- NCCN guidelines state an FDA approved biosimilar can be substituted for Herceptin. The guidelines do not specify what biosimilars are appropriate for a specific tumor type which allows for use of any of the biosimilars to be used for any indication the innovator product is FDA approved for.

References:

1. Herceptin [prescribing information]. South San Francisco, CA: Genentech, Inc.; February 2021.
2. Herzuma [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; May 2019.
3. Trazimera [prescribing information]. New York, NY: Pfizer; November 2020.
4. Kanjinti [prescribing information]. Thousand Oaks, CA: Pfizer; October 2022.
5. Ogivri [prescribing information]. Zurich, Switzerland: Mylan; July 2023.
6. Ontruzant [prescribing information]. Whitehouse Station, NJ: Merck and Co., Inc.; June 2021.
7. Stebbing J, Baranau Y, Baryash V, et al. CT-P6 compared with reference trastuzumab for HER2-positive breast cancer: a randomised, double-blind, active-controlled, phase 3 equivalence trial. Lancet Oncol. 2017 Jul; 18(7): 917-28.
8. Pegram MD, Bondarenko I, Zorzetto MMC, et al. PF-05280014 (a trastuzumab biosimilar) plus paclitaxel compared with reference trastuzumab plus paclitaxel for HER2-positive metastatic breast cancer: a randomized, double-blind study. BR J Cancer. 2019 Jan; 120(2): 172 – 82.
9. Von Minckwitz G, Colleoni M, Kolberg HC, et al. Efficacy and safety of ABP 980 compared with reference trastuzumab in women with HER2-positive early breast cancer (LILAC study): a randomised, double-blind, phase 3 trial. Lancet Onc. 2018 July 1; 19(7): 987 – 998.
10. National Comprehensive Cancer Network (NCCN). Breast cancer (Version 1.2024). 2024 Jan 25. Available from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed February 15, 2024.
11. National Comprehensive Cancer Network (NCCN). Gastric cancer (Version 3.2023). 2024 January 26. Available from: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed February 15, 2024.
12. Mylan Press Release. U.S. FDA Approves Mylan and Biocon's Ogivri, the First Biosimilar for Trastuzumab, for the Treatment of HER2- Positive Breast and Gastric Cancers. December 1, 2017. Available at: http://newsroom.mylan.com/2017-12-01-U-S-FDA-Approves-Mylan-and-Biocons-OgivriTM-the-First-Biosimilar-for-Trastuzumab-for-the-Treatment-of-HER2-Positive-Breast-and-GastricCancers
13. Rugo HS, Barve A, Waller CF, et al. Effect of a Proposed Trastuzumab Biosimilar Compared With Trastuzumab on Overall Response Rate in Patients With ERBB2 (HER2)–Positive Metastatic Breast Cancer A Randomized Clinical Trial. JAMA. 2017;317(1):37–47.
14. Pivot X, Bondarenko I, Nowecki Z, et al. Phase III, Randomized, Double-Blind Study Comparing the Efficacy, Safety, and Immunogenicity of SB3 (Trastuzumab Biosimilar) and Reference Trastuzumab in Patients Treated With Neoadjuvant Therapy for Human Epidermal Growth Factor Receptor 2–Positive Early Breast Cancer. J Clin Oncol. 2018; 36(10): 968 – 74.
15. National Comprehensive Cancer Network. Colon cancer (Version 1.2024). 2024 Jan 29. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed on February 15, 2024.

Policy History		
#	Date	Change Description
1.8	Effective Date: 04/11/2024	Annual review – no changes to the criteria at this time
1.7	Effective Date: 04/06/2023	Updated to include new indication of HER2-positive colorectal cancer
1.6	Effective Date: 02/02/2023	Updated approval length to allow for FDA recommended dosing for at least 60 days and up to 6 months at a time
1.5	Effective Date: 02/10/2022	Updated to remove prescriber requirement
1.4	Effective Date: 08/12/2021	Annual review of criteria was performed, no changes were made
1.3	Effective Date: 08/13/2020	New policy created for this class of drugs. The individual policies for Herzuma, Kanjinti, Ogivri, Ontruzant, and Trazimera will be retired.
1.2	Effective Date: 3/16/2020	UM medical management system update for MAPPO and BCNA for Kanjinti and Trazimera
1.1	Effective Date: 11/012019	UM medical management system update for BCN for Kanjiti, Trazimera, Herzuma, Ogivri and Ontruzant
1.0	Effective Date: 08/01/2019	UM medical management system update for BCN for Herceptin

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*