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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.

P&T Date: 08/07/2025

Herceptin Hylecta™ (trastuzumab and hyaluronidase-oysk)

HPCPS: J9356

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. FDA approved indication
 - b. Human epidermal growth factor receptor 2 (HER2) positive breast cancer defined as follows:
 - i. Immunohistochemistry (IHC) is 3+
OR
 - ii. In situ hybridization (ISH) positive by any of the following:
 - 1. Single probe average HER2 copy number greater than or equal to 6.0 signals/cell
OR
 - 2. Dual probe HER2/CEP17 ratio greater than or equal to 2.0
OR
 - 3. Dual probe HER2/CEP17 ratio less than 2.0 with an average HER2 copy number greater than or equal to 6.0 signals/cell
 - c. Must be used with concomitant treatment according to FDA indication or NCCN category 1 or 2A recommendation
 - d. Trial and failure, contraindication, or intolerance to intravenous trastuzumab
 - e. 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 treatment: Treatment continued until unacceptable toxicity or disease progression for up to a total of 52 weeks of therapy
 - ii. For metastatic disease: Treatment continued until unacceptable toxicity or disease progression

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

***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 Hylecta is a combination of trastuzumab and hyaluronidase indicated in adults for the treatment of HER2-overexpressing breast cancer.
- Per the 2024 National Comprehensive Cancer Network guidelines for breast cancer, patients are eligible for adjuvant HER2-directed treatment if they have HER2-positive breast cancer defined as:
 - Single probe average HER2 copy number greater than or equal to 6.0 signals/cell
OR
 - Dual probe HER2/CEP17 ratio greater than or equal to 2.0
OR
 - Dual probe HER2/CEP17 ratio less than 2.0 with an average HER2 copy number greater than or equal to 6.0 signals/cell
- The National Comprehensive Cancer Network (NCCN) guidelines category 1 and 2A recommendations are based on uniform NCCN consensus that the recommendations are appropriate. Treatment regimens have been studied and shown to be efficacious when administered as listed in the guidelines. Category 2B and 3 recommendations do not have a high level of evidence to support use and also do not have a uniform consensus from the NCCN panel that the recommendations are appropriate.

References:

1. Herceptin Hylecta [prescribing information]. South San Francisco, CA: Genentech, Inc; June 2024.
2. Jackisch C, Hegg R, Stroyakovskiy D, et al. HannaH phase III randomized study: association of total pathological complete response with event free survival in HER2-positive early breast cancer treated with neoadjuvant-adjuvant trastuzumab after 2 years of treatment-free follow-up. *Eur J Cancer*. 2016; 62: 62 – 75.
3. Gligorov J, Ataseven B, Verrill M, et al. Safety and tolerability of subcutaneous trastuzumab for the adjuvant treatment of human epidermal growth factor receptor-2 positive early breast cancer: SafeHer phase III study's primary analysis of 2573 patients. *Eur J Cancer*. 2017 Sept; 82: 237 – 46.
4. National Comprehensive Cancer Network (NCCN). Breast cancer (Version 4.2025). 2025 April 17. Available from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 10, 2024.

Policy History												
#	Date	Change Description										
1.9	P&T Date: 08/07/2025 Effective Date: 12/01/2025	Updated to include a step on intravenous trastuzumab										
1.8	Effective Date: 02/13/2025	Annual review of criteria was performed, no changes were made										
1.7	Effective Date: 02/08/2024	Annual review of criteria was performed, no changes were made										
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: 04/08/2021	Updated policy with NCCN guideline definition of HER2-positive breast cancer										
1.3	Effective Date: 12/01/2020	UM medical management system update for BCBS <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
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1.2	Effective Date: 04/16/2020	Annual review of criteria was performed, no changes were made										
1.1	Effective Date: 03/16/2020	UM medical management system update for MAPPO and BCNA <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	Yes	MAPPO	Yes	BCNA	Yes
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1.0	Effective Date: 05/09/2019	New Policy <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	Yes	MAPPO	No	BCNA	No
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* 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>.

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