CLINICAL MEDICATION POLICY	
Policy Name:	Herceptin® (trastuzumab)
Policy Number:	MD-023-MD-PA
Responsible Departments:	Medical Management Medical Policy; Clinical Pharmacy
Provider Notice Date:	06/01/2017
Original Effective Date:	07/01/2017
Annual Approval Date:	01/30/2018
Revision Date:	12/16/2016
Products:	Pennsylvania Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 8

Disclaimer

Gateway Health℠ (Gateway) clinical medication policy is intended to serve only as a general reference resource regarding payment and coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Gateway Health℠ may provide coverage under the medical or pharmacy benefits of the Company's Medicaid products for medically necessary intravenous infusions of Herceptin® (trastuzumab).

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

DEFINITIONS

Medical Necessity: A service or benefit is medically necessary if it is compensable under the Medical Assistance program and if it meets any one of the following standards:

- The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition, or disability
- The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental, or developmental effects of an illness, condition, injury, or disability.
- The service or benefit will assist the patient to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the patient and those functional capacities that are appropriate for patients of the same age.

Adjuvant Therapy – Refers to additional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biological therapy.

Metastatic Disease – The manifestation of a malignancy as a secondary growth arising from the primary growth in a new location. The malignant cells may spread via direct extension or through the lymphatic circulation, the bloodstream, or avenues such as the cerebrospinal fluid.

Monoclonal Antibody – An antibody specific to a certain antigen. Monoclonal antibodies are created in the laboratory.

Neoadjuvant Therapy – Refers to treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy. It is a type of induction therapy.

PROCEDURES

1. The following medical necessity criteria must be met for Herceptin:
    A. Coverage may be provided when the diagnosis is adjuvant breast cancer and the member meets the following criteria:
        1) The member is 18 years of age or older; AND
        2) The prescriber is a hematologist/oncologist; AND
        3) The member is not pregnant; AND
        4) There is baseline evaluation of left ventricular function prior to starting trastuzumab; AND
        5) The member has had HER2 testing using an FDA-approved test; AND
        6) The member is HER2 overexpressing node positive; OR
        7) The member has HER2 overexpressing node negative AND one of the following:
            a) ER/PR negative; OR
            b) Tumor size > 2cm; OR
            c) Member age is < 35 years; OR
            d) Histological and/or nuclear Grade 2 or 3; AND
        8) The member must be receiving one of the following regimens:

a) Trastuzumab as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; OR
b) Trastuzumab in combination with docetaxel and carboplatin; OR
c) Trastuzumab as a single agent following multi-modality anthracycline based therapy; AND

9) The dosing is within the following prescribing-supported parameter(s):
   a) During and following paclitaxel or docetaxel, as part of a treatment regimen containing doxorubicin and cyclophosphamide:
      1. Initial dose: 4 mg/kg IV one time
      2. Subsequent doses: 2 mg/kg IV weekly during paclitaxel or docetaxel for the first 12 weeks. One week following the last weekly dose of trastuzumab, administer trastuzumab 6 mg/kg IV every 3 weeks for a total of 52 weeks
   b) During and following docetaxel and carboplatin:
      1. Initial dose: 4 mg/kg IV one time
      2. Subsequent doses: 2 mg/kg IV weekly during docetaxel / carboplatin for the first 18 weeks. One week following the last weekly dose of trastuzumab, administer trastuzumab 6 mg/kg IV every 3 weeks for a total of 52 weeks
   c) Monotherapy, following anthracycline-based chemotherapy:
      1. Initial dose: 8 mg/kg IV one time
      2. Subsequent doses: 6 mg/kg IV every 3 weeks for a total of 52 weeks of trastuzumab therapy
   d) A total treatment duration of 12 months

B. Coverage may be provided when the diagnosis is metastatic breast cancer and the member meets the following criteria:
   1) The member is 18 years of age or older; AND
   2) The prescriber is a hematologist/oncologist; AND
   3) The member is not pregnant; AND
   4) The member has had HER2 testing using an FDA-approved test; AND
   5) The member has HER2 overexpressing metastatic disease; AND
   6) The drug is used in combination with paclitaxel for first-line therapy; OR
   7) The drug is being used as a single agent following one or more prior chemotherapy regimens; AND
   8) There is baseline evaluation of left ventricular function prior to starting trastuzumab; AND
   9) The dosing is within the following prescribing-supported parameters:
      a) Initial dose: 4 mg/kg IV one time
      b) Subsequent doses: 2 mg/kg IV once weekly

C. Coverage may be provided if the diagnosis is metastatic gastric cancer and the member meets the following criteria:
   1) The member is 18 years of age or older; AND
   2) The member is not pregnant; AND
   3) The prescriber is a hematologist/oncologist; AND
   4) The member has had HER2 testing using an FDA-approved test; AND

5) The member has HER2 overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma; AND
6) The member has not received prior treatment for metastatic disease; AND
7) The drug will be used in combination with cisplatin and capecitabine or 5-fluorouracil; AND
8) There is a baseline evaluation of left ventricular function prior to starting trastuzumab; AND
9) The dosing is within the following prescribing-supported parameters:
    a) Initial dose: 8 mg/kg IV one time
    b) Subsequent doses: 6 mg/kg IV every three weeks

Note: Chart documentation is required of the monitoring of left ventricular ejection fraction (LVEF) every three months as per the package insert.

2. When Herceptin is not covered
   Coverage may be provided for any non-FDA labeled indication or a medically accepted indication that is supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis for which it is prescribed and will be reviewed on a case-by-case basis to determine medical necessity.

   For conditions other than those listed above, scientific evidence has not been established, including but not limited to:
   A. HER2-negative breast cancer and other cancers which may be HER2 positive
   B. Osteosarcoma
   C. Non-small cell lung, ovarian, prostate, head and neck, esophageal cancers (except where noted above)
   D. Gastric, except for the condition noted above, pancreatic, colorectal, endometrial or urothelial cancers

3. Contraindications
   The safety and effectiveness of Herceptin in pediatric members has not been established.

4. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway Health℠ at any time pursuant to the terms of your provider agreement.

5. Place of Service
   The place of service for the administration of Herceptin is outpatient.

Governing Bodies Approval
Herceptin is a humanized monoclonal antibody against extracellular domain of HER2. Herceptin first received FDA approval in September 1998 for use in metastatic breast cancer, as a first-line therapy in combination with paclitaxel, and as a single agent in second- and third-line therapy.

The current FDA-approved labeling, as of May 2016, provides coverage for the use of Herceptin in the treatment of metastatic gastric or gastroesophageal junction adenocarcinoma, in

combination with cisplatin and capecitabine or 5-fluorouracil, in patients who have not received prior treatment for metastatic disease.

CODING REQUIREMENTS

Procedure Codes:

HCPCS Code	Description
J9355	Trastuzumab, 10 mg

Diagnosis Codes:

ICD-10 Codes	Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant right female breast

C50.512	Malignant neoplasm of lower-outer quadrant left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
D05.01	Lobular carcinoma in situ of right breast
D05.02	Lobular carcinoma in situ left breast
D05.11	Intraductal carcinoma in situ of right breast
D05.12	Intraductal carcinoma in situ of left breast
D05.81	Other specified type of carcinoma in situ of right breast
D05.82	Other specified type of carcinoma in situ of left breast
D05.91	Unspecified type of carcinoma in situ of right breast
D05.92	Unspecified type of carcinoma in situ of left breast
Z85.3	Personal history of malignant neoplasm of breast
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified

C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
D37.8	Neoplasm of uncertain behavior of other specified digestive organs (e.g., esophagus)
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
D00.2	Carcinoma in situ of stomach
D37.1	Neoplasm of uncertain behavior of stomach
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of unspecified esophagus
Z85.028	Personal history of other malignant neoplasm of stomach

REIMBURSEMENT

Participating facilities will be reimbursed per their Gateway Health℠ contract.

POLICY SOURCE(S)

Herceptin® [product information]. San Francisco, CA. Genentech; April 23, 2015. Accessed on May 27, 2016 and available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/103792s5327lbl.pdf.

NCCN Clinical Practice Guidelines in Oncology© 2014 National Comprehensive Cancer Network, Inc. For additional information, visit the NCCN website http://www.nccn.org. Accessed on May 27, 2016.

- Breast Cancer (V.3.2015)
- Breast Cancer (V.2.2016)
- Esophageal and Esophagogastric Junction Cancers (V.3.2015)
- Gastric Cancer (V.3.2015)
- Gastric Cancer (V.1.2016)
- Non-Small Cell Lung Cancer (V.7.2015)

Genentech, Inc. Herceptin (trastuzumab). Prescribing Information. South San Francisco, CA: Genentech; revised November 2006. Accessed June 14, 2016 and available at: http://www.gene.com/gene/products/information/pdf/herceptin-prescribing.pdf.

Wolff AC, Hammond EH, Schwartz JN, et al. American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer. J Clin Oncol. 2007; 25(1): 118-145. Accessed on August 25, 2016 and available at: http://www.quantason.com/pdf/breast_cancer/Human_Epidermal_Growth_Factor_Receptor_2.pdf.

Wolff AC, Hammond ME, Hicks DG, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. Arch Pathol Lab Med. 2014 Feb; 138(2):241-56. Accessed on August 25, 2016 and abstract available at: http://www.ncbi.nlm.nih.gov/pubmed/24099077.

Hammond EH, Hayes DF, and Wolff AC. Clinical Notice for American Society of Clinical Oncology-College of American Pathologists Guideline Recommendations on ER/PgR and HER2 Testing in Breast Cancer. J Clin Oncol. 2011; 29(15): e458. Accessed on August 25, 2016 and available at: http://www.jco.ascopubs.org/content/29/15/e458.full.pdf+html.

Policy History

Date	Activity
09/09/2016	Initial document developed
12/01/2016	Effective date
12/16/2016	Revisions: annual review, reference updates, indication and criteria updates, revised dosing **Criteria Changes:** • The pregnancy criteria was added for **ALL disease indications** - The member is not pregnant; • Testing criteria was added for **all disease indications** - The member has had HER2 testing using an FDA-approved test; • The drug regimen criteria for **adjuvant breast cancer** has been revised - OLD CRITERIA *The drug will be used in combination with a non-anthracycline containing regimen, and the dose does not exceed 8 mg/kg OR is not administered more frequently than once every week; OR The drug will be used as a single agent following anthracycline-based therapy, and the dose does not exceed 8 mg/kg OR is not administered more frequently than once every three weeks. The maximum treatment duration is twelve months.* NEW CRITERIA *Trastuzumab as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; OR Trastuzumab in combination with docetaxel and carboplatin; OR Trastuzumab as a single agent following multi-modality anthracycline based therapy;* • Dosage information has been updated for **ALL disease indications**
05/17/2017	QI UM Committee Review
07/01/2017	Provider effective date