**Draft Revision Policy: Do Not Implement**

**Trastuzumab Products: Trastuzumab (Herceptin®); Trastuzumab-dttb (Ontruzant®); Trastuzumab-pkrb (Herzuma®); Trastuzumab-dkst (Ogivri®); Trastuzumab-qyyp (Trazimera™); Trastuzumab-anns (Kanjinti™); Trastuzumab-strf (Hercessi™)**

Some agents on this policy may require step therapy See "Step Therapy Requirements for Provider Administered Specialty Medications" Document at:
https://www.bcbst.com/docs/providers/Comm_BC_PAD_Step_Therapy_Guide.pdf

**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 or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

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

**INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Adjuvant Breast Cancer
Adjuvant treatment of human epidermal growth factor receptor 2 (HER2)-overexpressing node positive or node negative (estrogen receptor [ER]/progesterone receptor [PR] negative or with one high risk feature) breast cancer

- as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
- as part of a treatment regimen with docetaxel and carboplatin
- as a single agent following multi-modality anthracycline based therapy

Metastatic Breast Cancer

- In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
- As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

Metastatic Gastric Cancer
In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease

Compendial Uses

- HER2-positive breast cancer
  - Neoadjuvant therapy
  - Treatment of recurrent, advanced, unresectable, or stage IV (M1) disease

    - Treatment for no response to preoperative systemic therapy
- Intra-cerebrospinal fluid (CSF) treatment for leptomeningeal metastases from HER2-positive breast cancer
- HER2-positive esophageal and esophagogastric junction cancer
- HER2-positive uterine serous carcinoma or ~~and~~ carcinosarcoma
- HER2-amplified/positive and RAS and BRAF wild-type colorectal cancer
- HER2-positive salivary gland tumor
- HER2-positive biliary tract cancers

All other indications are considered experimental/investigational and not medically necessary.

**DOCUMENTATION**

Submission of the following information is necessary to initiate the prior authorization review: human epidermal growth factor receptor 2 (HER2) status (where applicable), RAS mutation status (where applicable), BRAF mutation status (where applicable).

**COVERAGE CRITERIA**

**Breast Cancer**

Authorization of up to 12 months may be granted for neoadjuvant treatment of HER2-positive breast cancer as part of a complete treatment regimen.
Authorization of up to 12 months may be granted for adjuvant treatment of HER2-positive breast cancer.
Authorization of 12 months may be granted for treatment of HER2-positive breast cancer with no response to preoperative systemic therapy, recurrent, advanced, unresectable, or metastatic (including brain metastases) disease.
Authorization of 12 months may be granted for intra-CSF treatment for leptomeningeal metastases from HER2-positive breast cancer.

Authorization of 12 months may be granted for treatment of HER2-negative metastatic breast cancer when used in combination with neratinib and fulvestrant as third-line or later therapy.

**Esophageal, Gastric, or Gastroesophageal Junction Cancer**

Authorization of 12 months may be granted for treatment or palliative therapy of HER2-positive esophageal, gastric, or gastroesophageal ~~esophagogastric~~ junction cancer in combination with chemotherapy.

**Uterine Serous Carcinoma or Carcinosarcoma**

Authorization of 12 months may be granted for treatment of HER2-positive stage III-IV, recurrent, or metastatic uterine serous carcinoma or carcinosarcoma in combination with carboplatin and paclitaxel and continued as a single agent for maintenance therapy.

**Colorectal Cancer**

Authorization of 12 months may be granted for treatment of unresectable, advanced, or metastatic colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, when all of the following criteria are met:

- Member has HER2-positive/amplified disease.
- The disease is negative (wild-type) for RAS (KRAS and NRAS) and BRAF mutations.
- The requested medication will be used in combination with tucatinib, pertuzumab, or lapatinib.

- Member has received prior therapy for the disease or is not appropriate for intensive therapy.

**Salivary Gland Tumor**

Authorization of 12 months may be granted for treatment of recurrent, unresectable, or metastatic HER2-positive salivary gland tumors when used as a single agent or in combination with docetaxel or pertuzumab.

**Biliary Tract Cancers**

Authorization of 12 months may be granted for subsequent treatment of unresectable, resected gross residual (R2), or metastatic HER2-positive (IHC 3+/ISH +/NGS amplification) biliary tract cancers (including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer) when used in combination with pertuzumab or tucatinib.

**CONTINUATION OF THERAPY**

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant and neoadjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

**MEDICATION QUANTITY LIMITS**

| Drug Name | Diagnosis | Maximum Dosing Regimen |
|---|---|---|
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi<br>(Trastuzumab-strf) | Breast Cancer | Route of Administration: Intravenous<br>Initial: 4mg/kg once (7-day cycle)<br>Maintenance: 2 mg/kg every week<br><br>Initial: 8mg/kg once (21- day cycle)<br>Maintenance: 6 mg/kg every 3 weeks<br><br>4mg/kg once (7-day cycle), followed by 2 mg/kg every week through week 8, 12, or 18, then 6 mg/kg every 3 weeks to complete 52 weeks of therapy (Allowed up to 52 weeks of treatment for Adjuvant and Neo-adjuvant uses) |
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi<br>(Trastuzumab-strf) | CNS Cancer : Brain Metastases | Route of Administration: Intravenous<br>6mg/kg every week<br><br>Initial: 8mg/kg once (21-day cycle)<br>Maintenance: 6mg/kg every 3 weeks |
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi | CNS Cancers: Leptomeningeal Metastases | Route of Administration: Intrathecal, Intraventricular<br>150mg every week |

| | | |
|---|---|---|
| (Trastuzumab-strf) | | |
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi<br>(Trastuzumab-strf) | Colorectal Cancer, including or Appendiceal Adenocarcinoma and Anal Adenocarcinoma | Route of Administration: Intravenous<br>Initial 4mg/kg once (7-day cycle)<br>Maintenance: 2mg/kg every week<br><br>Initial:8mg/kg once (21-day cycle)<br>Maintenance: 6mg/kg every 3 weeks |
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi<br>(Trastuzumab-strf) | Esophageal Cancer, Esophagogastric Junction Cancer, or Gastric Cancer | Route of Administration: Intravenous<br>Initial: 8mg/kg once (21-day cycle)<br>Maintenance: 6mg/kg every 3 weeks<br><br>Initial: 6mg/kg once (14-day cycle)<br>Maintenance: 4mg/kg every 2 weeks |
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi<br>(Trastuzumab-strf) | Hepatobiliary Cancer, including Cholangiocarcinoma or Gallbladder Cancer | Route of Administration: Intravenous<br>Initial: 8mg/kg once (21-day cycle)<br>Maintenance: 6mg/kg every 3 weeks |
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi<br>(Trastuzumab-strf) | Salivary Gland Tumor | Route of Administration: Intravenous<br>Initial: 4mg/kg once (7 day cycle)<br>Maintenance: 2mg/kg every week<br><br>Initial: 8mg/kg once (21 day cycle)<br>Maintenance: 6mg/kg every 3 weeks |
| Herceptin (Trastuzumab)<br>Herzuma (Trastuzumab-pkrb)<br>Kanjinti (Trastuzumab-anns)<br>Ogivri (Trastuzumab-dkst)<br>Ontruzant (Trastuzumab-dttb)<br>Trazimera (Trastuzumab-qyyp)<br>Hercessi<br>(Trastuzumab-strf) | Uterine Neoplasms - Endometrial Carcinoma | Route of Administration: Intravenous<br>Initial: 8mg/kg once (21 day cycle)<br>Maintenance: 6mg/kg every 3 weeks |

## 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.

## 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).

**REFERENCES**

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**EFFECTIVE DATE**

ID_CHS_2025