Medical Policy:

Trastuzumab Injection (Herceptin®, Herceptin Hylecta®, Hercessi, Herzuma®, Kanjinti®, Ontruzant®, Ogivri®, Trazimera®)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.85	January 30, 2025	January 1, 2021

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Length of Authorization

Coverage will be provided for six months and may be renewed. Neoadjuvant and adjuvant treatment in Breast Cancer may be authorized up to a maximum of fifty-two (52) weeks of treatment.

Dosing Limits [Medical Benefit]

A. Max Units (per dose and over time):

	Indication	Load (1-time)	Load Billable Units (1-time)	Maintenance	Maintenance Billable Units	Interval (Days)
	Breast Cancer, Colorectal Cancer, Appendiceal Adenocarcinoma	4 mg/kg	45	2 mg/kg	30	7
		8 mg/kg	90	6 mg/kg	75	21
	Gastric, Esophageal, GEJ	6 mg/kg	75	4 mg/kg	45	14

Herceptin, Hercessi (150 mg SDV)	Cancer	8 mg/kg	90	6 mg/kg	75	21
	CNS metastases from Breast Cancer (in combination with capecitabine and tucatinib), Uterine Cancer, Head and Neck Cancer, Biliary Tract Cancers	8 mg/kg	90	6mg/kg	75	21
	CNS metastases from Breast Cancer (in combination with pertuzumab)	N/A	N/A	6mg/kg	75	7
	Leptomeningeal Metastases from Breast Cancer	N/A	N/A	100mg	15	7

	Indication	**Load (1-time)**	**Load Billable Units (1-time)**	**Maintenance**	**Maintenance Billable Units**	**Interval (Days)**
	Breast Cancer, Colorectal Cancer, Appendiceal Adenocarcinoma	4 mg/kg	46	2 mg/kg	23	7
		8 mg/kg	92	6 mg/kg	69	21
Ogivri, Kanjinti, Trazimera, Herzuma, Ontruzant (420 mg MDV)	Gastric, Esophageal, GEJ Cancer	6 mg/kg	69	4 mg/kg	46	14
		8 mg/kg	92	6 mg/kg	69	21
	CNS metastases from Breast Cancer (in combination with capecitabine and tucatinib), Uterine Cancer, Head and Neck Cancer, Biliary Tract Cancers	8 mg/kg	92	6 mg/kg	69	21
	CNS metastases from Breast Cancer (in combination with pertuzumab)	N/A	N/A	6mg/kg	69	7
	Leptomeningeal Metastases from Breast Cancer	N/A	N/A	100mg	10	7

Dosing and Administration

Please see package inserts

Guideline

For Commercial, Medicaid and Medicare members:

- Non-preferred agents: Herceptin, Herceptin Hylecta, Hercessi, Herzuma, Ontruzant, Ogivri
- Preferred agents: Kanjinti and Trazimera

I. Initial Approval Criteria

Coverage is provided in the following conditions *(in addition to use supported by the National Comprehensive Cancer Network [NCCN] Clinical Practice Guidelines [NCCN Guidelines®] and/or NCCN Drugs & Biologics Compendium [NCCN Compendium®] with a recommendation of category level 1 or 2A*):*

1. Baseline left ventricular ejection fraction (LVEF) within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
2. Patient is 18 years or older; **AND**
3. Patient's cancer is human epidermal growth factor receptor 2 (HER2)-positive*****; **AND**
4. For <u>newly started therapy</u> with a non-preferred agent (Herceptin, Herceptin Hylecta, Hercessi, Herzuma, Ontruzant, or Ogivri), for Commercial, Medicaid, and Medicare members:

   Coverage may be considered medically necessary when:

   a. Patient has experienced a therapeutic failure or intolerance with the plan-preferred medications (Kanjinti AND Trazimera); **OR**
   b. The non-preferred agent is requested for an indication for which the plan-preferred biosimilar agents (Kanjinti or Trazimera) have not been FDA-approved OR are not supported by NCCN Guidelines® or NCCN Compendium® with a recommendation of category level 1 or 2A; **AND**

**<u>Please note:</u> Coverage for an appropriate biosimilar substitution will be allowed where NCCN Guidelines or Compendium state that an FDA-approved biosimilar is an appropriate substitution for trastuzumab.*

<u>Breast cancer †</u>

1. Used as adjuvant therapy; **AND**

   A. Patient has locally advanced, node positive, or inflammatory disease; **AND**

      i. Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) with or without pertuzumab; **OR**

      ii. Used as a single agent; **OR**

      iii. Used in combination with pertuzumab; **OR**
2. Used as neoadjuvant or preoperative therapy; **AND**

   A. Patient has locally advanced, node positive, or inflammatory disease; **AND**

   B. Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) with or without pertuzumab; **OR**
3. Used for recurrent unresectable or metastatic disease **OR** inflammatory breast cancer; **AND**

   A. Used as a single agent in patients who have received one or more prior chemotherapy regimens for metastatic disease †; **OR**

   B. Used in combination with one of the following:

      i. Paclitaxel as first-line therapy for metastatic disease †

      ii. Endocrine therapy (e.g., tamoxifen, fulvestrant, or aromatase inhibition with or without lapatinib) in patients with hormone-receptor positive disease; **AND**

         a. Patient is post-menopausal; **OR**

         b. Patient is pre-menopausal and is treated with ovarian ablation/suppression; **OR**

         c. Patient is premenopausal and will not receive ovarian ablation/suppression (with tamoxifen ONLY); **OR**

         d. Patient is a male (sex assigned at birth)

      iii. Pertuzumab and a taxane (e.g., docetaxel, paclitaxel) as first-line therapy

      iv. Capecitabine and tucatinib as second-line therapy and beyond

v. Cytotoxic chemotherapy as third-line therapy and beyond
vi. Lapatinib (without cytotoxic therapy) as third-line therapy and beyond
vii. Pertuzumab with or without cytotoxic therapy as subsequent therapy in patients previously treated with chemotherapy and trastuzumab (without pertuzumab)

Central Nervous System Cancer ‡

1. Patient has leptomeningeal metastases from breast cancer; **AND**
   A. Herceptin will be administered intrathecally; **OR**
2. Patient has brain metastases from breast cancer; **AND**
   A. Used in combination with ONE of the following:
      i. Pertuzumab
      ii. Capecitabine and tucatinib in patients previously treated with at least one HER2-directed regimen; **AND**
   B. Used in ONE of the following treatment settings:
      i. Used as initial treatment in patients with small asymptomatic brain metastases
      ii. Patient has recurrent limited brain metastases
      iii. Patient has recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options
      iv. Patient has relapsed limited brain metastases with either stable systemic disease or reasonable systemic treatment options

Gastric, Esophageal and Esophagogastric Junction Cancers †

1. Patient is not a surgical candidate or has unresectable locally advanced, recurrent, or metastatic adenocarcinoma; **AND**
2. Used as first-line therapy in combination with chemotherapy with or without pembrolizumab

Endometrial Carcinoma- Uterine Cancer ‡

1. Used in combination with carboplatin and paclitaxel; **AND**
2. Used for advanced or recurrent uterine serous carcinoma; **AND**
   A. Patient has stage III/IV disease; **OR**
   B. Patient has recurrent disease and has not received prior trastuzumab therapy

Colorectal Cancer (CRC) ‡

1. Patient has RAS and BRAF wild-type (WT) disease; **AND**
2. Used in combination with pertuzumab, lapatinib, or tucatinib; **AND**
   A. Used as initial treatment for unresectable metastatic disease and previous FOLFOX or CapeOX within the past 12 months; **AND**
      i. Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
      ii. Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for immunotherapy *(Note: Only applies to Colon Cancer);* **OR**

B. Used as primary treatment for unresectable (or medically inoperable), locally advanced, or metastatic disease if intensive therapy is not recommended; **AND**
   i. Patient has not previously received HER2-directed therapy; **AND**
   ii. Used in one of the following:
      a. Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
      b. Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**

C. 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; **AND**
   i. Patient has not previously received HER2-directed therapy; **AND**
   ii. Used in one of the following:
      a. Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
      b. Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy

Appendiceal Adenocarcinoma – Colon Cancer‡

1. Patient has RAS and BRAF wild-type (WT) disease; **AND**
2. Used in combination with pertuzumab, lapatinib, or tucatinib; **AND**
3. Patient has not previously received HER2-targeted therapy; **AND**
4. Used for one of the following:
   A. Used as initial therapy for advanced or metastatic disease if intensive therapy is not recommended; **OR**
   B. 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; **AND**
5. Used in one of the following:
   A. Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
   B. Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease **AND** is not a candidate for or has progressed on checkpoint inhibitor immunotherapy

Head and Neck Cancer ‡

1. Patient has salivary gland tumors; **AND**
2. Used as a single agent OR in combination with either docetaxel or pertuzumab; **AND**
3. Patient has recurrent disease with one of the following:
   A. Distant metastases
   B. Unresectable locoregional recurrence with prior radiation therapy (RT)
   C. Unresectable second primary with prior RT

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) ‡

1. Used as subsequent treatment for progression on or after systemic treatment for unresectable, resected gross residual (R2), or metastatic disease; **AND**

2. Used in combination with pertuzumab

† FDA Approved Indication(s); ‡ Compendia recommended Indication(s)

*HER2-positive overexpression criteria
Breast, CNS, Uterine, Head and Neck, and Biliary Tract Cancer:
• 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 of the following: o HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; OR o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; OR o o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+
Gastric, Esophageal, and Esophagogastric Junction Cancer:
• Gastric, Esophageal, and Esophagogastric Junction Cancer: 32,33,48 • Immunohistochemistry (IHC) assay 3+; OR • Fluorescence in situ hybridization (FISH) or in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following: o HER2/CEP17 ratio ≥ 2.0 AND concurrent IHC 2+; OR o o Average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+
Colorectal Cancer and Appendiceal Adenocarcinoma:
• Immunohistochemistry (IHC) assay 3+; OR • Fluorescence in situ hybridization (FISH) HER2/CEP17 ratio ≥ 2 AND concurrent IHC 2+; OR o Next-generation sequencing (NGS) panel HER2 amplification

II. Renewal Criteria

Coverage can be renewed based upon the following criteria:

1. Continuation of documented current and/or successful therapy with a non-preferred agent (Herceptin, Herceptin Hylecta, Hercessi, Herzuma, Ontruzant or Ogivri); **AND**
2. Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**
3. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: cardiotoxicity (i.e. left ventricular dysfunction, cardiomyopathy); pulmonary toxicity (i.e. pneumonitis); neutropenia; infusion-related reactions; etc.; **AND**
4. Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows:
   - LVEF is within the institutional normal limits, and has not had an absolute decrease of ≥ 16% from pre-treatment baseline; **OR**
   - LVEF is below the institutional lower limits of normal, and has not had an absolute decrease of ≥ 10% from pre-treatment baseline; **AND**

Breast Cancer (neoadjuvant and adjuvant therapy)

1. Patient has not exceeded a maximum of fifty-two (52) weeks of treatment (total 18 cycles)

Applicable Procedure Codes

Code	Description
J9355	Injection, trastuzumab, 10 mg; 1 billable unit = 10mg

J9356	Herceptin Hylecta (injection, trastuzumab 10 mg and hyaluronidase-oysk) 600-10000 MG-UNT/5ML SOLN
Q5113	Injection, trastuzumab-pkrb, biosimilar, (Herzuma), 10 mg
Q5114	Injection, Trastuzumab-dkst, biosimilar, (Ogivri), 10 mg
Q5112	Injection, trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg
Q5116	Injection, trastuzumab-qyyp, biosimilar, (trazimera), 10 mg, effective 10/01/2019
Q5117	Injection, trastuzumab-anns, biosimilar, (kanjinti), 10 mg, effective 10/01/2019
Q5146	Injection, trastuzumab-strf, biosimilar (hercessi) 10mg

Applicable NDCs

Code	Description
50242-0132-xx	Herceptin 150 mg SDV; powder for injection
50242-0077-01	Herceptin Hylecta 600 mg/10,000 units providing 600 mg trastuzumab and 10,000 units hyaluronidase per 5 mL.
63459-0305-xx	Herzuma (trastuzumab-pkrb) for Injection 420 mg/vial, multi-dose vial
63459-0303-xx	Injection, Trastuzumab-pkrb, biosimilar, (Herzuma), 10 mg 150mg SDV
67457-0847-xx	Ogivri (trastuzumab-dkst) for injection 420 mg/vial, multi-dose vial, with diluent
67457-0845-xx	Injection, Trastuzumab-dkst, biosimilar, (Ogivri), 10 mg, 420 mg/vial, multi-dose vial, without diluent
67457-0991-xx	Injection, Trastuzumab-dkst, biosimilar, (Ogivri), 10 mg, 150mg SDV
78206-0147-xx	Injection, Trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg 150 mg/vial, single-dose vial
78206-0148-xx	Injection, Trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg 420mg MDV
55513-0132-01	vial, 1 each Trastuzumab (Kanjinti) 420mg, Lyophilisate for solution for injection, no diluent
55513-0164-xx	Injection, trastuzumab-anns, biosimilar, (Kanjinti), 10 mg 420mg with diluent
55513-0141-xx	Injection, trastuzumab-anns, biosimilar, (Kanjinti), 10 mg 150mg SDV
00069-0305-01	Trazimera (trastuzumab-qyyp) injection 420 mg/vial, multiple-dose vial
00069-0308-xx	Injection, trastuzumab-qyyp, biosimilar, (Trazimera), 10 mg 150mg SDV
69338-0015-05	Injection, trastuzumab-strf, biosimilar, (Hercessi), 150mg single dose vial
69448-0016-xx	Injection, trastuzumab-strf, biosimilar, (Hercessi), 420mg MDV

ICD-10 Diagnoses

Code	Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of the 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
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 female breast
C50.021	Malignant neoplasm of nipple and areola, right female breast
C50.022	Malignant neoplasm of nipple and areola, left female breast
C50.029	Malignant neoplasm of nipple and areola, unspecified female 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 of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of 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
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C79.32	Secondary malignant neoplasm of cerebral meninges
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
Z80.49	Family history of malignant neoplasm of other genital organs
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.3	Personal history of malignant neoplasm of breast

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/15/2025	Added Hercessi to policy and criteria as non-preferred agent
EmblemHealth & ConnectiCare	10/28/2024	Annual Review: Updated length of authorization statement to include: Neoadjuvant and adjuvant treatment in Breast Cancer may be authorized up to a maximum of fifty-two (52) weeks of treatment. (previously only in renewal criteria) Updated dosing limit charts. Breast cancer Initial Criteria: added: Patient is premenopausal and will not receive ovarian ablation/suppression (with tamoxifen ONLY); OR Gastric, Esophageal and Esophagogastric Junction Cancers Removed: (excluding use in combination with DCF [docetaxel, carboplatin, and fluorouracil])" Endometrial Carcinoma- Uterine Cancer- updated name and added: Patient has stage III/IV disease; OR Patient has recurrent disease and has not received prior trastuzumab therapy Added the following indications and criteria: Colorectal Cancer (CRC) Appendiceal Adenocarcinoma – Colon Cancer‡ Head and Neck Cancer Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) Updated *HER2-positive overexpression criteria chart

		Reworded: "Left ventricular ejection fraction (LVEF) has not had an absolute decrease of more than 15% from baseline and is within normal limits" to Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows: LVEF is within the institutional normal limits, and has not had an absolute decrease of ≥ 16% from pre-treatment baseline; OR LVEF is below the institutional lower limits of normal, and has not had an absolute decrease of ≥ 10% from pre-treatment baseline; AND Removed all: Limitations/Exclusions Updated Jcode and NDCs
EmblemHealth & ConnectiCare	10/27/2023	Update: Effective 1/1/2024 Removed Ogivri as preferred agent, added to non-preferred agents.
EmblemHealth & ConnectiCare	9/25/2023	Annual Review: Initial Criteria: Added: prior to initiating therapy and will be assessed at regular intervals (e.g., every 3months during treatment, AND" to the following istatement: Baseline left ventricular ejection fraction (LVEF) within normal limits "prior to initiating therapy and will be assessed at regular intervals (e.g., every 3months during treatment, AND" <u>Breast cancer</u> Initial Criteria: Removed: "Used as adjuvant treatment; OR 1. Used as preoperative treatment for breast preservation; OR 2. Used for recurrent or metastatic disease" Added: 1. "Used as adjuvant therapy; AND A. Patient has locally advanced, node positive, or inflammatory disease; AND i. Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) with or without pertuzumab; OR ii. Used as a single agent; OR B. Used in combination with pertuzumab; OR 2. Used as neoadjuvant or preoperative therapy; AND A. Patient has locally advanced, node positive, or inflammatory disease; AND B. Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) with or without pertuzumab; OR 3. Used for recurrent unresectable or metastatic disease OR inflammatory breast cancer; AND A. Used as a single agent in patients who have received one or more prior chemotherapy regimens for metastatic disease †; OR B. Used in combination with one of the following: i. Paclitaxel as first-line therapy for metastatic disease † ii. Endocrine therapy (e.g., tamoxifen, fulvestrant, or aromatase inhibition with or without lapatinib) in patients with hormone-receptor positive disease; AND a. Patient is post-menopausal; OR b. Patient is pre-menopausal and is treated with ovarian ablation/suppression; OR c. Patient is a male (sex assigned at birth) iii. Pertuzumab and a taxane (e.g., docetaxel, paclitaxel) as first-line therapy C. Capecitabine and tucatinib as second-line therapy and beyond D. Cytotoxic chemotherapy as third-line therapy and beyond

		E. Lapatinib (without cytotoxic therapy) as third-line therapy and beyond F. Pertuzumab with or without cytotoxic therapy as subsequent therapy in patients previously treated with chemotherapy and trastuzumab (without pertuzumab)" Central Nervous System Cancer Initial Criteria: Added 3. "Patient has brain metastases from breast cancer; AND D. Used in combination with ONE of the following: iii. Pertuzumab iv. Capecitabine and tucatinib in patients previously treated with at least one HER2-directed regimen; AND E. Used in ONE of the following treatment settings: v. Used as initial treatment in patients with small asymptomatic brain metastases vi. Patient has recurrent limited brain metastases vii. Patient has recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options viii. Patient has relapsed limited brain metastases with either stable systemic disease or reasonable systemic treatment options" Gastric, Esophageal and Esophagogastric Junction Cancers Initial Criteria: Removed: 1. "Used in combination with cisplatin and 5-FU or capecitabine for first-line therapy; AND 2. Patient has metastatic disease" Added: 3. "Patient is not a surgical candidate or has unresectable locally advanced, recurrent, or metastatic adenocarcinoma; AND 4. Used as first-line therapy in combination with chemotherapy with or without pembrolizumab (excluding use in combination with DCF [docetaxel, carboplatin, and fluorouracil])" Renewal Criteria: Added: Breast Cancer (neoadjuvant and adjuvant therapy) Patient has not exceeded a maximum of fifty-two (52) weeks of treatment (total 18 cycles)
EmblemHealth & ConnectiCare	1/17/2023	Transfer to New Template
EmblemHealth & ConnectiCare	12/19/2020	Clarifications: • Step therapy will apply to NEW starts only • NCCN-supported use (with 1 or 2A recommendation) will be covered Renewal criteria updated: • Removed: "Patient continues to meet criteria identified above" Added coverage: "Continuation of documented current and/or successful therapy with a non-preferred agent (Herceptin, Herceptin Hylecta, Herzuma, or Ontruzant)."
EmblemHealth & ConnectiCare	11/2/2020	Effective **01/01/2021**, Member must fail trial of Kanjinti, Ogivri, and Trazimera, prior to using Herceptin, Herceptin Hylecta, Herzuma, or Ontruzant. (Medicare members are subject to this step therapy).
EmblemHealth & ConnectiCare	03/31/2020	Added to the Initial Criteria: Effective 07/01/2020, Kanjinti, Ogivri, and Trazimera are the preferred agents for Commercial and Medicaid members. Member must fail trial of Kanjinti AND Ogivri AND Trazimera

		prior to using Herceptin, Herceptin Hylecta, Herzuma, and Ontruzant (Only Commercial and Medicaid members are subject to this step therapy).
EmblemHealth & ConnectiCare	03/31/2020	Updated covered indications for Herceptin Hylecta, Herzuma, Kanjinti, Ogivri, Ontruzant, and Trazimera per FDA label
EmblemHealth & ConnectiCare	09/23/2019	Updated Policy to include Kanjinti and Trazimera. Added New codes for Kanjinti Q5117 and Trazimera Q5116.
EmblemHealth & ConnectiCare	9/13/2019	Updated Indication for Herzuma to include metastatic gastric or gastroesophageal junction adenocarcinoma.
EmblemHealth & ConnectiCare	7/1/2019	Added Herceptin Hylecta, Herzuma, Ogivri, and Ontruzant
EmblemHealth & ConnectiCare	1/1/2021	New Policy

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