Trastuzumab:
Herceptin®; Ogivri®; Kanjinti™; Trazimera™; Herzuma®; Ontruzant®
(Intravenous)

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I. Length of Authorization [1-6]

Coverage is provided for 6 months and may be renewed (unless otherwise specified).

- Neoadjuvant and adjuvant therapy in Breast Cancer may be authorized up to a maximum of fifty-two (52) weeks of therapy.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 150 mg single-dose vial: 6 vials day 1, then 5 vials every 21 days thereafter
- 420 mg multiple-dose vial: 3 vials day 1, then 2 vials every 21 days thereafter

B. Max Units (per dose and over time) [HCPCS Unit]:

	Indication	Load (1-time)	Load Billable Units (1-time)	Maint.	Maint. Billable Units	Interval (Days)
Herceptin (150 mg SDV)	Breast Cancer; Colorectal Cancer	4 mg/kg	45	2 mg/kg	30	7
		8 mg/kg	90	6 mg/kg	75	21
	Gastric; Esophageal; GEJ Cancer	6 mg/kg	75	4 mg/kg	45	14
		8 mg/kg	90	6 mg/kg	75	21
	CNS mets from Breast Cancer, Uterine Cancer, Head and Neck Cancer	8 mg/kg	90	6 mg/kg	75	21

	Indication	Load (1-time)	Load Billable Units (1-time)	Maint.	Maint. Billable Units	Interval (Days)
Ogivri, **Kanjinti**, **Trazimera**, **Herzuma**, **Ontruzant** (420 mg MDV)	Breast Cancer; Colorectal Cancer	4 mg/kg	46	2 mg/kg	23	7
		8 mg/kg	92	6 mg/kg	69	21
	Gastric; Esophageal; GEJ Cancer	6 mg/kg	69	4 mg/kg	46	14
		8 mg/kg	92	6 mg/kg	69	21
	CNS mets from Breast Cancer, Uterine Cancer, Head and Neck Cancer	8 mg/kg	92	6 mg/kg	69	21

III. Initial Approval Criteria [1-6]

The preferred trastuzumab products are Kanjinti and Trazimera.

Requests for an alternative trastuzumab product may be considered medically necessary if:

- Patient has experienced a therapeutic failure or intolerance with Kanjinti AND Trazimera; **OR**
- The alternative trastuzumab product is requested for an indication for which Kanjinti AND Trazimera have not been FDA-approved

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1-6]

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Therapy will not be substituted with or for ado-trastuzumab emtansine (Kadcyla) or fam-trastuzumab deruxtecan-nxki (Enhertu); **AND**
- Therapy will not be used in combination with trastuzumab and hyaluronidase-oysk (Herceptin Hylecta) or pertuzumab/trastuzumab and hyaluronidase-zzxf (Phesgo); **AND**

Breast Cancer † ‡ [1-6,8,10-16,35-38,43,44,10e,11e,13e,14e,16e,17e,19e,20e]

- Used as adjuvant therapy; **AND**
  - Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel) †; **OR**
  - Used as a single agent following chemotherapy; **OR**
  - Used in combination with pertuzumab for node positive (N1-N3) disease; **OR**
- Used as neoadjuvant or preoperative therapy; **AND**
  - Patient has locally advanced, node positive, or inflammatory disease; **AND**
  - Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) with or without pertuzumab; **OR**
- Used for recurrent unresectable or metastatic disease; **AND**
  - Used as a single agent in patients who have received one or more prior chemotherapy regimens for metastatic disease †; **OR**
  - Used as first-line therapy in combination with paclitaxel †; **OR**
  - Used in combination with endocrine therapy (e.g., tamoxifen, fulvestrant, or aromatase inhibition with or without lapatinib) in patients with hormone-receptor positive disease; **AND**

- Patient is post-menopausal; **OR**
- Patient is pre-menopausal and is treated with ovarian ablation/suppression; **OR**
- Patient is a male receiving concomitant suppression of testicular steroidogenesis; **OR**

- Used in combination with one of the following:
  - Pertuzumab and a taxane (e.g., docetaxel, paclitaxel) as first-line therapy
  - Capecitabine and tucatinib as third-line therapy and beyond after prior HER2-directed therapy with trastuzumab, pertuzumab, AND ado-trastuzumab emtansine, unless there is a contraindication or intolerance
  - Cytotoxic chemotherapy as third-line therapy and beyond
  - Lapatinib (without cytotoxic therapy) as third-line therapy and beyond after prior anti-HER2 directed therapy for metastatic disease
  - Pertuzumab with or without cytotoxic therapy as subsequent therapy in patients previously treated with chemotherapy and trastuzumab (without pertuzumab); **AND**

    Subsequent therapy in combination with pertuzumab with or without cytotoxic therapy *(does NOT apply to second-line therapy)*:
    - Use of trastuzumab in combination with pertuzumab with or without cytotoxic therapy will be restricted to patients with a contraindication or intolerance to lapatinib/capecitabine, trastuzumab/lapatinib, or a regimen containing trastuzumab in combination with a generically available agent (e.g., trastuzumab/capecitabine, etc. [*see NCCN Breast Cancer guidelines for complete list of alternative regimens*])

Central Nervous System Cancer ‡ [7,18,29,30]

- Patient has brain metastases from breast cancer; **AND**
  - Used in combination with capecitabine and tucatinib; **AND**
  - Patient has previously been treated with trastuzumab, pertuzumab, AND ado-trastuzumab; **AND**
    - Used as initial treatment in patients with small asymptomatic brain metastases; **OR**
    - Patient has recurrent limited brain metastases; **OR**
    - Patient has recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options; **OR**
    - Patient has relapsed limited brain metastases with either stable systemic disease or reasonable systemic treatment options

Gastric, Esophageal and Esophagogastric Junction Cancers † Φ [1-7,17,32,33,34e,35e]

- Patient has unresectable (or medically inoperable) locally advanced, recurrent, or metastatic adenocarcinoma; **AND**
- Used as first-line therapy in combination with oxaliplatin or cisplatin AND fluorouracil or capecitabine (with or without pembrolizumab)

Uterine Cancer (Endometrial Carcinoma) ‡ [7,19,34]

- Used in combination with carboplatin and paclitaxel; **AND**
- Patient has advanced (stage III/IV) or recurrent uterine serous carcinoma

Colorectal Cancer ‡ [7,9,31,21e,22e]

- Patient has RAS and BRAF wild-type (WT) disease; **AND**
- Used in combination with pertuzumab or lapatinib; **AND**
- Patient has not previously received HER2-directed therapy; **AND**
  - 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**

In combination with pertuzumab only:

- Use of trastuzumab in combination with pertuzumab will be restricted to patients with a contraindication or intolerance to trastuzumab/lapatinib

Head and Neck Cancer ‡ [7,39-42]

- Patient has salivary gland tumors; **AND**
- Used in combination with docetaxel or pertuzumab; **AND**
- Used for one of the following:
  - Recurrent disease with distant metastases; **OR**
  - Unresectable locoregional recurrence with prior radiation therapy (RT); **OR**
  - Recurrent unresectable second primary with prior RT; **AND**

In combination with pertuzumab only:

- Use of trastuzumab in combination with pertuzumab will be restricted to patients with a contraindication or intolerance to trastuzumab/docetaxel

***HER2-positive overexpression criteria:** [8,10]

- 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:

- HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; **OR**
- HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; **OR**
- HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

❖ *If confirmed using an immunotherapy assay-http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-9]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: cardiotoxicity (e.g., left ventricular dysfunction, cardiomyopathy), pulmonary toxicity (e.g., dyspnea, interstitial pneumonitis), neutropenia, infusion-related reactions, etc.; **AND**
- Left ventricular ejection fraction (LVEF) 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 (adjuvant and neoadjuvant therapy)

- Patient has not exceeded a maximum of fifty-two (52) weeks of therapy

V. Dosage/Administration [1-9,18,19,29,31-33,40-42]

Indication	Dose
Breast Cancer	Neoadjuvant/Adjuvant Therapy Combination Therapy

	–Administer an initial dose of 4 mg/kg intravenously followed by 2 mg/kg intravenously weekly during chemotherapy for up to 18 weeks. –One week following the last weekly dose of trastuzumab, administer 6 mg/kg intravenously every three weeks. **OR** –Administer an initial dose of 4 mg/kg intravenously followed by 2 mg/kg intravenously weekly. **OR** –Administer an initial dose at 8 mg/kg intravenously followed by 6 mg/kg intravenously every three weeks. Single-Agent Therapy (following anthracycline therapy) –Administer an initial dose at 8 mg/kg intravenously, followed by subsequent doses at 6 mg/kg intravenously every three weeks. *Note: Therapy should not exceed a total of 52 weeks of treatment.* **Recurrent or Metastatic Disease (alone or in combination with chemotherapy)** Loading dose: 4 mg/kg intravenously x 1 for every 7-day dosing schedule Maintenance dose: 2 mg/kg intravenously every 7 days **OR** Loading dose: 8 mg/kg intravenously x 1 for every 21-day dosing schedule Maintenance dose: 6 mg/kg every 21 days *Note: Treat until disease progression or intolerable toxicity.*
Gastric, Esophageal and Esophagogastric Junction Cancers	Loading dose: 8 mg/kg intravenously x 1 for every 21-day dosing schedule Maintenance dose: 6 mg/kg intravenously every 21 days **OR** Loading dose: 6 mg/kg intravenously x 1 for every 14-day dosing schedule Maintenance dose: 4 mg/kg intravenously every 14 days *Note: Treat until disease progression or intolerable toxicity.*
Colorectal Cancer	Loading dose: 8 mg/kg intravenously x 1 for every 21-day dosing schedule Maintenance dose: 6 mg/kg intravenously every 21 days **OR** Loading dose: 4 mg/kg intravenously x 1 for every 7-day dosing schedule Maintenance dose: 2 mg/kg intravenously every 7 days *Note: Treat until disease progression or intolerable toxicity.*
CNS Metastases from Breast Cancer	Loading dose: 8 mg/kg intravenously x 1 for every 21-day dosing schedule Maintenance dose: 6 mg/kg intravenously every 21 days *Note: Treat until disease progression or intolerable toxicity.*
Uterine Cancer	Loading dose: 8 mg/kg intravenously x 1 for every 21-day dosing schedule Maintenance dose: 6 mg/kg intravenously every 21 days

	Note: Treat until disease progression or intolerable toxicity.
Head and Neck Cancer	Loading dose: 8 mg/kg intravenously x 1 for every 21-day dosing schedule Maintenance dose: 6 mg/kg intravenously every 21 days *Note: Treat until disease progression or intolerable toxicity.*

VI. Billing Code/Availability Information

Brand Name	HCPCS	HCPCS Description	1 BU	Vial Size & Type	NDCs
Herceptin	J9355	Injection, trastuzumab, excludes biosimilar, 10 mg	10 mg	150 mg SDV	50242-0132-xx
				420 mg MDV *(discontinued)*	50242-0333-xx *(discontinued)*
Ogivri	Q5114	Injection, Trastuzumab-dkst, biosimilar, (Ogivri), 10 mg	10 mg	150 mg SDV	67457-0991-xx
				420 mg MDV (with diluent)	67457-0847-xx
				420 mg MDV (no diluent)	67457-0845-xx
Kanjinti	Q5117	Injection, trastuzumab-anns, biosimilar, (Kanjinti), 10 mg	10 mg	150 mg SDV	55513-0141-xx
				420 mg MDV	55513-0132-xx
Trazimera	Q5116	Injection, trastuzumab-qyyp, biosimilar, (Trazimera), 10 mg	10 mg	150 mg SDV	00069-0308-xx
				420 mg MDV	00069-0305-xx
Herzuma	Q5113	Injection, Trastuzumab-pkrb, biosimilar, (Herzuma), 10 mg	10 mg	150 mg SDV	63459-0303-xx
				420 mg MDV	63459-0305-xx
Ontruzant	Q5112	Injection, Trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg	10 mg	150 mg SDV	78206-0147-xx
				420 mg MDV	78206-0148-xx

Notes:
- Herceptin is only available as a single-dose vial; therefore, the JW modifier is allowed
- Ogivri, Kanjinti, Trazimera, Herzuma, & Ontruzant are available as both single-dose and multi-dose vials. Approvals are based upon use of the MDV; therefore, the JW modifier is not allowed

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C06.9	Malignant neoplasm of mouth, unspecified
C07	Malignant neoplasm of parotid gland
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C08.9	Malignant neoplasm of major salivary gland, unspecified
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

ICD-10	ICD-10 Description
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
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
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

ICD-10	ICD-10 Description
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

ICD-10	ICD-10 Description
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
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31	Secondary malignant neoplasm of brain
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
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.3	Personal history of malignant neoplasm of breast

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD):

Jurisdiction(s): N(9)	**NCD/LCD/LCA Document (s):** A56660
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56660&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA,HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC