Independent Health

Ontruzant® (trastuzumab-dttb)
(Intravenous)

Document Number: IC-0432

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I. Length of Authorization

Coverage is provided for six months and may be renewed.

- Use for neo-adjuvant and adjuvant breast cancer is limited to a total of 52 weeks of treatment

II. Dosing Limits

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

– Ontruzant 150 mg single-dose vial: 7 vials every 21 days

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

Breast Cancer and Gastric/Esophageal/Gastro-esophageal junction Cancers

	Load (billable units)	Maintenance (billable units)
7-day dosing schedule	45	30
21-day dosing schedule	90	75

CNS Cancer

- 15 billable units every 7 days

Uterine Cancer

- 90 billable units, followed by 75 billable units every 21 days

III. Initial Approval Criteria[1]

Coverage is provided in the following conditions:

- Baseline left ventricular ejection fraction (LVEF) within normal limits; **AND**
- Patient is 18 years or older; **AND**
- Patient's cancer is human epidermal growth factor receptor 2 (HER2)-positive*; **AND**

Breast cancer †[1,2, 5-10]

- Used as adjuvant therapy in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) OR as a single agent following anthracycline-based therapy; **OR**

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- Used as neoadjuvant therapy for breast preservation in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.); **OR**
- Used for recurrent or metastatic disease; **AND**
  - Used as a single agent in patients who have received one or more prior treatments for metastatic disease †; **OR**
  - Used in first-line therapy in combination with paclitaxel†; **OR**
  - Used in combination with endocrine therapy 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 cytotoxic chemotherapy OR lapatinib OR pertuzumab and a taxane as first-line therapy OR pertuzumab as subsequent therapy in patients who were previously treated with trastuzumab without pertuzumab; **AND**
    - Disease is hormone receptor-negative; **OR**
    - Disease is hormone receptor-positive and used with or without endocrine therapy

Central Nervous System Cancer ‡[2,12]

- Patient has leptomeningeal metastases from breast cancer; **AND**
- Trastuzumab will be administered intrathecally

Gastric, Esophageal and Esophagogastric Junction Cancers †[1,2,11]

- Used in combination with cisplatin and 5-FU or capecitabine for first-line therapy; **AND**
- Patient has metastatic adenocarcinoma

Uterine Cancer ‡[2,13]

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

Colorectal Cancer ‡[2,14]

- Used as subsequent therapy for progression of unresectable advanced or metastatic RAS WT disease; **AND**
- Must be used in combination with pertuzumab or lapatinib in patients who have not previously received HER2-targeted therapy; **AND**

Patient must have been previously treated with FOLFOXIRI, oxaliplatin-based therapy without irinotecan, irinotecan-based therapy without oxaliplatin, or fluoropyrimidine-based therapy without irinotecan or oxaliplatin

***HER2-positive overexpression criteria:** [3,4]

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- Immunohistochemistry (IHC) assay 3+; **OR**
- Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0AND 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+

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

IV. Renewal Criteria[1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria 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 the following: cardiotoxicity (e.g., left ventricular dysfunction, cardiomyopathy, etc.); pulmonary toxicity (i.e., pneumonitis); neutropenia; infusion-related reactions; etc.; **AND**
  - LVEF has not had an <u>absolute</u> decrease of ≥ 16% from pre-treatment baseline and is within the institutional normal limits; **OR**
  - LVEF has not had an <u>absolute</u> decrease of ≥ 10% from pre-treatment baseline and is below the institutional lower limits of normal; **AND**
- Use for neoadjuvant and adjuvant breast cancer treatment is limited to a total of 52 weeks of therapy

V. Dosage/Administration

Indication	Dose
Breast Cancer	<u>**Combination Therapy**</u> –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. *Note: Neo-adjuvant/Adjuvant therapy should not exceed a total of 52 weeks of treatment.* <u>**Single-Agent Therapy (following anthracycline therapy)**</u>

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	–Administer an initial dose at 8 mg/kg intravenously, followed by subsequent doses at 6 mg/kg intravenously every three weeks. *Note: Neo-adjuvant/Adjuvant therapy should not exceed a total of 52 weeks of treatment.* **Metastatic Disease (alone or in combination with chemotherapy)** Administer at an initial dose of 4 mg/kg intravenously followed by subsequent once weekly doses of 2 mg/kg intravenously until disease progression. **OR** Loading dose: 8 mg/kg x 1 for every 21 day dosing schedule Maintenance dose: 6 mg/kg every 21 days
Gastric, Esophageal and Esophagogastric Junction Cancers	Loading dose: 8 mg/kg x 1 for every 21 day dosing schedule Maintenance dose: 6 mg/kg every 21 days **OR** Loading dose: 4 mg/kg x 1 for weekly dosing schedule Maintenance dose: 2 mg/kg every 7 days *Note: Treat until disease progression or intolerable toxicity.*
Leptomeningeal Metastases from Breast Cancer	Escalating doses up to 100 mg intrathecally weekly.* **Dosing is highly variable and should be individualized.* *Note: Treat until disease progression or intolerable toxicity.*
Uterine & Colorectal Cancers	Loading dose: 8 mg/kg x 1 for every 21 days dosing schedule Maintenance dose: 6 mg/kg every 21 days *Note: Treat until disease progression or intolerable toxicity.*

VI. Billing Code/Availability Information

HCPCS code:

- Q5112 – Injection, Trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg; 1 billable unit = 10 mg

NDC:

- Ontruzant 150 mg single-dose vial; powder for injection: 00006-5033-xx

VII. References

1. Ontruzant [package insert]. Yeonsu-gu, Incheon, Republic of Korea; Samsung Bioepsis; January 2019. Accessed November 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) trastuzumab. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2019.

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3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 3.2019. National Comprehensive Cancer Network, 2019. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed October 2019.
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13. Fader AN, Roque DM, Siegel E, et al. Randomized Phase II Trial of Carboplatin-Paclitaxel Versus Carboplatin-Paclitaxel-Trastuzumab in Uterine Serous Carcinomas That Overexpress Human Epidermal Growth Factor Receptor 2/neu. J Clin Oncol. 2018 Jul 10;36(20):2044-2051. doi: 10.1200/JCO.2017.76.5966. Epub 2018 Mar 27.

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 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
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum

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ICD-10	ICD-10 Description
C17.2	Malignant neoplasm ileum
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, 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
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

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ICD-10	ICD-10 Description
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

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ICD-10	ICD-10 Description
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
C79.32	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
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
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) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

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

Jurisdiction(s): J(10); M(11)	**NCD/LCD Document (s):** A56141
https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=56141&ver=30&Date=10%2f31%2f2019&DocID=A56141&bc=hAAAABAAAAAA&	

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Jurisdiction(s): N(9)	**NCD/LCD Document (s):** A56660
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?Date=10/30/2019&DocID=A56660&bc=hAAAAAAAAAAA&	

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

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