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

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I. Length of Authorization [1-6]

Coverage is provided for six months and may be renewed.

- Use in the neo-adjuvant and adjuvant setting is limited to a total of 52 weeks of treatment.

II. Dosing Limits

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

- Herceptin 150 mg single-dose vial: 7 vials every 21 days
- Herceptin 420 mg multiple-dose vial: 3 vials every 21 days
- Ogivri 150 mg single-dose vial: 7 vials every 21 days
- Ogivri 420 mg multiple-dose vial: 3 vials every 21 days
- Kanjinti 150 mg single-dose vial: 7 vials every 21 days
- Kanjinti 420 mg multiple-dose vial: 3 vials every 21 days
- Trazimera 420 mg multiple-dose vial: 3 vials every 21 days
- Herzuma 150 mg single-dose vial: 7 vials every 21 days
- Herzuma 420 mg multiple-dose vial: 3 vials every 21 days
- Ontruzant 150 mg single-dose vial: 7 vials every 21 days
- Ontruzant 420 mg multiple-dose vial: 3 vials every 21 days

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

Breast Cancer & Colorectal Cancer

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

Gastric/Esophageal/Gastro-esophageal Junction Cancers

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

CNS Cancer (Leptomeningeal metastases from breast cancer)

- 15 billable units every 7 days

CNS Cancer (Limited/Extensive brain metastases) & Uterine Cancer

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

III. Initial Approval Criteria [1-6]

Coverage is provided in the following conditions:

- Patient must have a contraindication or intolerance or documented history of failure to a biosimilar trastuzumab prior to consideration of Herceptin; **AND**
- 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**
- Will not be used in combination with trastuzumab and hyaluronidase-oysk (Herceptin Hylecta) or pertuzumab/trastuzumab and hyaluronidase-zzxf (Phesgo); **AND**

Breast Cancer † [1-68,10-16,35-38]

- Used as adjuvant therapy; **AND**
  - Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) †; **OR**
  - Used as a single agent following chemotherapy; **OR**
  - Used in combination with pertuzumab for locally advanced or node positive disease; **OR**
- Used as neoadjuvant or preoperative therapy for locally advanced disease or node positive disease; **AND**
  - Used in combination with a taxane-based regimen (e.g., docetaxel, paclitaxel, etc.) with or without pertuzumab; **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 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:
  - cytotoxic chemotherapy
  - lapatinib (without cytotoxic therapy)
  - capecitabine plus tucatinib *(includes use in advanced unresectable disease)* in patients who have received one or more lines of prior HER2-targeted therapy in the metastatic setting
  - pertuzumab and a taxane (e.g., docetaxel, paclitaxel) as first-line therapy
  - pertuzumab with or without cytotoxic therapy as one line of therapy beyond first-line therapy in patients who were previously treated with trastuzumab without pertuzumab

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

- Patient has leptomeningeal metastases from breast cancer; **AND**
  - Trastuzumab will be administered intrathecally; **OR**
- Patient has limited or extensive brain metastases from breast cancer; **AND**
  - Used in combination with capecitabine and tucatinib; **AND**
  - Patient previously received at least one HER2-directed therapy; **AND**
    - Used as primary treatment in patients with small asymptomatic brain metastases; **OR**
    - Used for relapsed disease in patients with limited brain metastases who are systemically stable or have other reasonable systemic treatment options; **OR**
    - Used for recurrent limited brain metastases; **OR**
    - Used for recurrent disease in patients with extensive brain metastases who are systemically stable or have other reasonable systemic treatment options

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

- Used in combination with chemotherapy *(excluding use with anthracyclines or in combination with DCF [docetaxel, carboplatin, and fluorouracil])* as first-line therapy; **AND**
- Patient has metastatic adenocarcinoma

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 Adenocarcinoma ‡ [7,9,31]

- Used in combination with pertuzumab or lapatinib in patients who have not previously received HER2-targeted therapy; **AND**
- Patient has RAS and BRAF wild-type (WT) disease; **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; **OR**
  - Patient is not appropriate for intensive therapy; **AND**
    - Used as initial systemic therapy for locally unresectable (or medically inoperable) or metastatic disease; **OR**
    - Used for unresectable or metastatic disease that remains unresectable after primary treatment; **OR**
    - Used for metastatic disease in patients who have received adjuvant FOLFOX or CapeOX more than 12 months ago OR who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy

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

- 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+

❖ *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 can be renewed based upon the following criteria:

- Patient continues to meet 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 the following: cardiotoxicity (e.g., left ventricular dysfunction, cardiomyopathy, etc.), pulmonary toxicity (e.g., dyspnea, interstitial pneumonitis, etc.), neutropenia, infusion-related reactions, etc.; **AND**
  - LVEF is within the institutional normal limits, but has not had an absolute decrease of ≥ 16% from pre-treatment baseline (LVEF results must be within the previous 3 months); **OR**
  - LVEF is below the institutional lower limits of normal, but has not had an absolute decrease of ≥ 10% from pre-treatment baseline (LVEF results must be within the previous 3 months); **AND**
- Use for neoadjuvant and adjuvant breast cancer treatment is limited to a total of 52 weeks of therapy

V. Dosage/Administration [1-9,18,29]

Indication	Dose
Breast Cancer	**Neo-adjuvant/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. 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.*
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.*
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.*

VI. Billing Code/Availability Information

HCPCS Code:

- J9355 - Injection, trastuzumab, excludes biosimilar, 10 mg; 1 billable unit (bu) = 10 mg
- Q5114 – Injection, Trastuzumab-dkst, biosimilar, (Ogivri), 10 mg; 1 bu = 10 mg
- Q5117 - Injection, trastuzumab-anns, biosimilar, (Kanjinti), 10 mg: 1 bu = 10 mg
- Q5116 – Injection, trastuzumab-qyyp, biosimilar, (Trazimera), 10 mg; 1 bu = 10 mg
- Q5113 – Injection, Trastuzumab-pkrb, biosimilar, (Herzuma), 10 mg; 1 bu = 10 mg
- Q5112 – Injection, Trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg; 1 bu = 10 mg

NDC(s):

- Herceptin 150 mg single-dose vial; powder for injection: 50242-0132-xx
- Herceptin 420 mg multiple-dose vial; powder for injection: 50242-0333-xx*
- Ogivri 150 mg single-dose vial; powder for injection: 67457-0991-xx
- Ogivri 420 mg multiple-dose vial; powder for injection: 67457-0847-xx
- Kanjinti 150 mg single-dose vial powder for injection: 55513-0141-xx
- Kanjinti 420 mg multiple-dose vial; powder for injection: 55513-0132-xx
- Trazimera 420 mg multiple-dose vial; lyophilized powder for injection: 00069-0305-xx
- Herzuma 150 mg single-dose vial; powder for injection: 63459-0303-xx
- Herzuma 420 mg multiple-dose vial: powder for injection: 63459-0305-xx
- Ontruzant 150 mg single-dose vial; powder for injection: 00006-5033-xx
- Ontruzant 420 mg multiple-dose vial; powder for injection: 00006-5034-xx

**Note: Not commercially available*

VII. References

1. Herceptin [package insert]. South San Francisco, CA; Genentech, Inc; November 2018. Accessed October 2020.
2. Ogivri [package insert]. Steinhausen, SZ; Mylan, Inc; June 2020. Accessed October 2020.
3. Kanjinti [package insert]. Thousand Oaks, CA; Amgen, Inc; October 2019. Accessed October 2020.
4. Trazimera [package insert]. Cork, Ireland; Pfizer Ireland, Inc; November 2019. Accessed October 2020.
5. Herzuma [package insert]. Yeonsu-gu, Incheon, Republic of Korea; Celltrion, Inc; May 2019. Accessed October 2020.
6. Ontruzant [package insert]. Yeonsu-gu, Incheon, Republic of Korea; Samsung Bioepsis; March 2020. Accessed October 2020.
7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) trastuzumab. National Comprehensive Cancer Network, 2020. 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 October 2020.
8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 6.2020. National Comprehensive Cancer Network, 2020. 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 2020.
9. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer 4.2020. National Comprehensive Cancer Network, 2020. 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 2020.
10. Wolff AC, Hammond EH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol 2018;36:2105-2122.
11. Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Engl J Med. 2005;353:1673-1684 and supplementary appendix.
12. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. N Engl J Med. 2005;353:1659-1672.
13. Cameron D, Piccart-Gebhart MJ, Gelber RD et al. 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: final analysis of the HERceptin Adjuvant (HERA) trial. Lancet. 2017 Mar 25;389(10075):1195-1205.

14. Vogel CL, Cobleigh MA, Tripathy D, et al. Efficacy and safety of trastuzumab as a single agent in first-line treatment of HER2-overexpressing metastatic breast cancer. J Clin Oncol. 2002 Feb 1;20(3):719-26.
15. Seidman AD, Berry D, Cirrincione C, et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all HER-2 overexpressors and random assignment to trastuzumab or not in HER-2 nonoverexpressors: final results of Cancer and Leukemia Group B protocol 9840. J Clin Oncol. 2008 Apr 1;26(10):1642-9.
16. Robert N, Leyland-Jones B, Asmar L, et al. Randomized phase III study of trastuzumab, paclitaxel, and carboplatin compared with trastuzumab and paclitaxel in women with HER-2-overexpressing metastatic breast cancer.
17. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-esophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet. 2010 Aug 28;376(9742):687-97. J Clin Oncol. 2006 Jun 20;24(18):2786-92.
18. Zagouri F, Sergentanis TN, Bartsch R, et al. Intrathecal administration of trastuzumab for the treatment of meningeal carcinomatosis in HER2-positive metastatic breast cancer: a systematic review and pooled analysis. Breast Cancer Res Treat 2013; 139:13-22.
19. 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.
20. Hainsworth JD, Meric-Bernstam F, Swanton C, et al. Targeted Therapy for Advanced Solid Tumors on the Basis of Molecular Profiles: Results From MyPathway, an Open-Label, Phase IIa Multiple Basket Study. Clin Oncol. 2018 Feb 20;36(6):536-542.
21. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
22. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
23. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
24. von Minckwitz G, Colleoni M, Kolberg HC, et al. Efficacy and safety of ABP 980 compared with reference trastuzumab in women with HER2-positive early breast cancer (LILAC study): a randomised, double-blind, phase 3 trial. Lancet Oncol. 2018;19:987-998.
25. Rugo HS, Barve A, Waller CF, et al. Effect of a proposed trastuzumab biosimilar compared with trastuzumab on overall response rate in patients with ERBB2 (HER2)-positive metastatic breast cancer: a randomized clinical trial. JAMA. 2017;317:37–47.
26. Pivot X, Bondarenko I, Nowecki Z, et al. Phase III, randomized, double-blind study comparing the efficacy, safety, and immunogenicity of SB3 (trastuzumab biosimilar) and

reference trastuzumab in patients treated with neoadjuvant therapy for human epidermal growth factor receptor 2-positive early breast cancer. J Clin Oncol. 2018;36:968-974.

27. Pegram MD, Bondarenko I, Zorzetto MMC, et al. PF-05280014 (a trastuzumab biosimilar) plus paclitaxel compared with reference trastuzumab plus paclitaxel for HER2-positive metastatic breast cancer: a randomised, double-blind study. Br J Cancer. 2019;120:172-182.
28. Esteva FJ, Baranau YV, Baryash V, et al. Efficacy and safety of CT-P6 versus reference trastuzumab in HER2-positive early breast cancer: updated results of a randomised phase 3 trial. Cancer Chemother Pharmacol. 2019 Oct;84(4):839-847.
29. Murthy RK, Loi S, Okines A, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. N Engl J Med.2020;382:597-609.
30. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers 3.2020. National Comprehensive Cancer Network, 2020. 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 August 2020.
31. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer 6.2020. National Comprehensive Cancer Network, 2020. 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 2020.
32. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer 3.2020. National Comprehensive Cancer Network, 2020. 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 2020.
33. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers 4.2020. National Comprehensive Cancer Network, 2020. 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 2020.
34. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Uterine Neoplasms 1.2021. National Comprehensive Cancer Network, 2020. 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 2020.

35. Perez EA, Romond EH, Suman VJ, et al. Trastuzumab plus adjuvant chemotherapy for human epidermal growth factor receptor 2-positive breast cancer: planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831. J Clin Oncol. 2014;32(33):3744-3752.
36. Slamon D, Eiermann W, Robert N, et al. Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med. 2011;365(14):1273-1283.
37. Eiermann W; International Herceptin Study Group. Trastuzumab combined with chemotherapy for the treatment of HER2-positive metastatic breast cancer: pivotal trial data. Ann Oncol. 2001;12 Suppl 1:S57-S62.
38. Cobleigh MA, Vogel CL, Tripathy D, et al. Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. J Clin Oncol. 1999;17(9):2639-2648.
39. First Coast Service Options, Inc. Local Coverage Article: Billing and Coding: Trastuzumab - Trastuzumab Biologics (A56660). Centers for Medicare & Medicaid Services, Inc. Updated on 07/22/2020 with effective date of 07/01/2020. Accessed October 2020.
40. Palmetto GBA. Local Coverage Article: Billing and Coding: Chemotherapy (A56141). Centers for Medicare & Medicaid Services, Inc. Updated on 05/26/2020 with effective date of 4/30/2020. Accessed October 2020.

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

ICD-10	ICD-10 Description
C17.1	Malignant neoplasm jejunum
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

ICD-10	ICD-10 Description
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

ICD-10	ICD-10 Description
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
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), 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: 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/LCA/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&	

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