

## Enhertu<sup>®</sup> (fam-trastuzumab deruxtecan-nxki) (Intravenous)

Document Number: IC-0522

Last Review Date: 02/02/2021

Date of Origin: 02/04/2020

Dates Reviewed: 02/2020, 06/2020, 09/2020, 02/2021

### I. Length of Authorization

Coverage will be provided for six months and may be renewed.

### II. Dosing Limits

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

- Enhertu 100 mg vial: 7 vials every 21 days

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

- Breast Cancer: 600 billable units every 21 days
- All other indications: 700 billable units every 21 days

### III. Initial Approval Criteria <sup>1</sup>

Coverage is provided in the following conditions:

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

#### Universal Criteria <sup>1</sup>

- 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; **AND**
- Used as single agent therapy; **AND**
- Therapy will not be substituted with or for any trastuzumab-based formulation (i.e., trastuzumab [or trastuzumab biosimilar product], ado-trastuzumab emtansine, trastuzumab-hyaluronidase, pertuzumab/trastuzumab and hyaluronidase-zzxf, etc.); **AND**

#### Breast Cancer † ‡ <sup>1,2,4,8</sup>

- Patient has recurrent, unresectable, or metastatic disease; **AND**
- Patient has previously been treated with at least two (2) prior HER2-targeted therapies for metastatic disease

#### Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma † <sup>1,9</sup>

- Patient has locally advanced or metastatic disease; **AND**
- Patient has previously been treated with a trastuzumab-based regimen

## Colorectal Adenocarcinoma †<sup>2,10-12</sup>

- 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

## Non-Small Cell Lung Cancer (NSCLC) †<sup>2,13,14</sup>

- Patient has metastatic disease

† FDA approved indication(s); ‡ Compendia Recommended Indication(s); Ⓢ Orphan Drug

### \*HER2-positive overexpression criteria:<sup>4,5</sup>

- Immunohistochemistry (IHC) assay 3+; **OR**
- Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio  $\geq 2.0$  AND average HER2 copy number  $\geq 4.0$  signals/cell; **OR**
- Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following:
  - HER2/CEP17 ratio  $\geq 2.0$  AND average HER2 copy number  $< 4.0$  signals/cell AND concurrent IHC 3+; **OR**
  - HER2/CEP17 ratio  $< 2.0$  AND average HER2 copy number  $\geq 6.0$  signals/cell AND concurrent IHC 2+ or 3+; **OR**
  - HER2/CEP17 ratio  $< 2.0$  AND average HER2 copy number  $\geq 4.0$  and  $< 6.0$  signals/cell AND concurrent IHC 3+

## IV. Renewal Criteria<sup>1,10,13</sup>

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: left ventricular dysfunction/symptomatic congestive heart failure, pulmonary toxicity (i.e., interstitial lung disease/pneumonitis), neutropenia/febrile neutropenia, etc.; **AND**

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- LVEF is > 45% and absolute decrease is ≤ 20% from baseline (LVEF results must be within the previous 3 months); **OR**
- LVEF is 40% to 45% and absolute decrease is < 10% from baseline (LVEF results must be within the previous 3 months)

## V. Dosage/Administration <sup>1,11-13</sup>

Indication	Dose
Breast Cancer	Administer 5.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
Gastric/Gastroesophageal Junction (GEJ) Adenocarcinoma	Administer 6.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
Colorectal Adenocarcinoma	Administer 6.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
Non-Small Cell Lung Cancer	Administer 6.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity

## VI. Billing Code/Availability Information

### HCPCS Code:

- J9358 – Injection, fam-trastuzumab deruxtecan-nxki, 1 mg: 1 billable unit = 1 mg

### NDC:

- Enhertu 100 mg single-dose vial: 65597-0406-xx

## VII. References

1. Enhertu [package insert]. Basking Ridge, NJ; Daiichi Sankyo, Inc; January 2021. Accessed January 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) fam-trastuzumab deruxtecan. National Comprehensive Cancer Network, 2021. 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 January 2021.
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10. Siena S, Di Bartolomeo M, Raghav KPS, et al. A phase II, multicenter, open-label study of trastuzumab deruxtecan in patients with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01. *J Clin Oncol* 2020;38(suppl; abstr 4000).
11. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer 1.2021. National Comprehensive Cancer Network, 2021. 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 January 2021.
12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer 1.2021. National Comprehensive Cancer Network, 2021. 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 January 2021.
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14. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer 2.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer

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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 of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.8	Malignant neoplasm of overlapping sites of small intestine
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 colon

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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
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
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 male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male 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

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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

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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
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
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
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

## 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 Determinations (LCDs), and Local Coverage Articles (LCAs) 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/LCA):

<b>Jurisdiction(s):</b> N(9)	<b>NCD/LCD/LCA Document (s):</b> A56660
<a href="https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56660&amp;bc=EAAAAAAAAAAAA&amp;SearchType=Advanced">https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56660&amp;bc=EAAAAAAAAAAAA&amp;SearchType=Advanced</a>	

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)

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
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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