Medical Policy:

Enhertu® (fam-trastuzumab deruxtecan-nxki) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.210	March 18, 2024	April 6, 2020

Definitions

Fam-trastuzumab deruxtecan-nxki is a HER2-directed antibody-drug conjugate. The antibody is a humanized anti-HER2 IgG1. The small molecule DXd, is a topoisomerase I inhibitor attached to the antibody by a cleavable linker. Following binding to HER2 on tumor cells, fam-trastuzumab deruxtecan-nxki undergoes internalization and intracellular linker cleavage by lysosomal enzymes. Upon release, the membrane-permeable DXd causes DNA damage and apoptotic cell death.

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

5.4mg/kg/every 3 weeks (21-day cycle)

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

- Breast Cancer, NSCLC: 600 Billable Units Every 21 Days
- All Other Indications: 700 Billable Units Every 21 Days

Guideline

I. Initial Approval Criteria

Enhertu may be considered medically necessary if the below conditions are met AND use is consistent with the medical necessity criteria that follows:

1. Patient is 18 years of age and older; **AND**
2. Baseline left ventricular ejection fraction (LVEF) within normal limits; **AND**

1. Breast cancer †

A. Patient's disease is unresectable or metastatic; **AND**
B. Patient's cancer is human epidermal growth factor receptor 2 (HER2)-positive; **AND**
C. Patient has received a prior anti-HER2-based regimen either:
   i. in the metastatic setting; **OR**
   ii. in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy.

2. HER2-Low Metastatic Breast Cancer

A. Patient has unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-approved test; **AND**
B. Patient has received a prior chemotherapy in the metastatic setting **OR** developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

3. Unresectable or Metastatic HER2-Mutant Non-Small Cell Lung Cancer

A. Patient has unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test; **AND**
B. Patient has received a prior systemic therapy.

4. Locally Advanced or Metastatic Gastric Cancer

A. Patient has locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma; **AND**
B. Patient has received a prior trastuzumab-based regimen

Limitations/Exclusions

Enhertu is considered investigational when used for any indication not listed above.

II. Renewal Criteria

Coverage can be renewed based upon the following criteria:

1. Patient continues to meet initial approval criteria; **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) has not had an absolute decrease of more than 20% from baseline and is within normal limits

Dosage/Administration

	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 Cancer	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 5.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity

Applicable Procedure Codes

Code	Description
J9358	Injection, fam-trastuzumab deruxtecan-nxki, 1 mg (Enhertu)

Applicable NDCs

Code	Description
65597-0406-01	Enhertu 100 mg single-dose vial

ICD-10 Diagnoses

Code	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
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 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
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
Z85.3	Personal history of malignant neoplasm of breast
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	3/18/2024	Annual Review: No criteria changes
EmblemHealth & ConnectiCare	07/06/2023	Annual Review: Initial Approval Criteria: Removed "3. Patient's cancer is human epidermal growth factor receptor 2 (HER2)-positive" and moved it under Breast Cancer. Breast Cancer: Initial Criteria Removed "Patient has received 2 or more prior anti-HER2-based regimens in the metastatic setting." Added "Patient's cancer is human epidermal growth factor receptor 2 (HER2)-positive; **AND** Patient has received a prior anti-HER2-based regimen either: iii. in the metastatic setting; **OR** iv. in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy." Added: HER2-Low Metastatic Breast Cancer Indication, Unresectable or Metastatic HER2-Mutant Non-Small Cell Lung Cancer Indication and Locally Advanced or Metastatic Gastric Cancer Indication Updated dosing chart Added Codes:

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C16.4	Malignant neoplasm of pylorus
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		C78.01	Secondary malignant neoplasm of right lung
		C78.02	Secondary malignant neoplasm of left lung
		Z85.028	Personal history of other malignant neoplasm of stomach
		Z85.118	Personal history of other malignant neoplasm of bronchus and lung
EmblemHealth & ConnectiCare	04/21/2022	Transferred policy to new template	
EmblemHealth & ConnectiCare	06/11/2020	Added J-Code (J9358) Injection, fam-trastuzumab deruxtecan-nxki, 1 mg (Enhertu). Effective Date: 07/01/2020	
EmblemHealth & ConnectiCare	04/06/2020	New Medical Policy	

References

1. Product Information: ENHERTU® intravenous injection, fam-trastuzumab deruxtecan-nxki intravenous injection. Daiichi Sankyo Inc (per FDA), Basking Ridge, NJ, 2019.
2. NIOSH: The National Institute for Occupational Safety and Health (NIOSH): NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. National Institute for Occupational Safety and Health (NIOSH). Cincinnati, OH. 2020. Available from URL: https://www.cdc.g... . As accessed 2020-03-20.
3. Centers for Disease Control and Prevention (CDC): NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. Centers for Disease Control and Prevention (CDC). Atlanta, GA. 2016. Available from URL: http://www.cdc.go... . As accessed 2016-11-03.