Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Fam-trastuzumab deruxtecan-nxki (Enhertu)	MP-RX-FP-180-26	☒ **MMM MA** ☒ **MMM MultiHealth**	03/23/2026 **Last Review Date:** 03/24/2026	03/24/2026 **Frequently Revision:** Annual

Service Category:

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other: Part B Drugs

Service Description:

This document addresses the use of Enhertu® (fam-trastuzumab deruxtecan-nxki), a drug approved by the Food and Drug Administration (FDA) for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer (IHC 3+ or ISH+), as determined by an FDA-approved test, including in combination with pertuzumab as first-line therapy.

Background Information:

This document addresses the use of Enhertu (fam-trastuzumab deruxtecan-nxki). Enhertu is HER2-directed antibody and topoisomerase inhibitor conjugate that selectively delivers chemotherapy to HER2-overexpressing tumor cells. Internalization and intracellular linker cleavage of the drug by lysosomal enzymes within the tumor cell leads to DNA damage and apoptotic cell death.

Breast cancer is a type of tumor comprised of malignant (cancerous) cells that start to grow in the breast and may spread (metastasize) to surrounding tissues and other areas of the body (American Cancer Society, 2016). Breast cancer is commonly treated by various modalities which include combinations of surgery, radiation therapy, chemotherapy and hormone therapy (National Cancer Institute, 2019). The prognosis and selection of therapies can be affected by clinical and pathologic features of the tumor. One of these includes the human epidermal growth factor receptor 2 gene ERBB2 which is commonly referred to as HER2. Other names for this gene include NEU, Her-2, HER-2/neu and c-erb B2. Initially the HER2 gene was detected in frozen breast tumor samples. Amplification of the HER2 gene was later correlated to overexpression of protein levels in samples of breast cancer.

Approximately 255,000 patients are diagnosed with invasive breast cancer each year, with approximately one in five cases being classified as HER-2 positive. Antibody-drug conjugates containing trastuzumab and a second non-specific cytotoxic drug have the ability to more specifically target HER-2 cancer cells and exert their anti-tumor effects. Kadcyla and Enhertu are currently the only two HER2-directed antibody-drug conjugates on the market. Kadcyla is linked to emtansine, a tubulin inhibitor, whereas Enhertu is linked to DXd, a topoisomerase inhibitor.

The FDA approved indications for Enhertu include:

- HER2-positive metastatic breast cancer
- HER2-low and ultralow metastatic breast cancer
- HER2-mutant unresectable or metastatic non-small cell lung cancer
- HER2-positive locally advanced or metastatic gastric cancer
- HER2-positive (IHC-3+) unresectable or metastatic solid tumors

Enhertu has a black box warning for interstitial lung disease and embryo-fetal toxicity. Interstitial lung disease (ILD) and pneumonitis, including fata cases, have been reported with Enhertu. Patients should be monitored for

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			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Enhertu should be discontinued in all patients with Grade 2 or higher ILD/pneumonitis.

The National Comprehensive Cancer Network® (NCCN) clinical practice guideline for central nervous system cancers, provides a 2A recommendation is provided for use as a single agent treatment for asymptomatic brain metastases in those with HER 2+ breast cancer. Subgroup analysis from the ongoing open-label phase II DESTINY-Breast01 trial showed that the antibody-drug conjugate famtrastuzumab deruxtecan-nxki (deruxtecan being a DNA topoisomerase 1 inhibitor) was associated with a 58% ORR in 24 patients with asymptomatic brain metastases from HER2-positive breast cancer who were previously treated with ado-trastuzumab emtansine.568 Partial intracranial responses were observed in 41%. In the multicenter open label randomized phase III DESTINY-Breast03 trial, in which fam trastuzumab deruxtecan-nxki is being compared to ado-trastuzumab emtansine in patients with metastatic HER2-positive breast cancer previously treated with trastuzumab and a taxane, results presented at an annual meeting showed that median PFS was significantly greater in the fam-trastuzumab deruxtecan-nxki arm, compared to the ado-trastuzumab emtansine arm (15.0 months vs. 5.7 months, respectively; HR, 0.38; 95% CI, 0.23–0.64) (Cortes J et.al. 2021).

In the NCCN clinical practice guideline for colon cancer and rectal cancer the NCCN Panel now recommends use of Enhertu (category level 2A) in the treatment of individuals with HER2 mutations in these cancers based on recent published abstracts from small phase 2 trials (Siena S 2020, Smit EF 2020). The data demonstrating safety and efficacy from these trials have not been published. At this time, there is no evidence to support the safety and efficacy of Enhertu in these solid tumors cancers.

NCCN also provides a category 2A recommendation in cervical cancer and endometrial cancer as second-line or subsequent therapy as a single agent in HER2-positive tumors (IHC 3+ or 2+) in local/regional recurrence or stage IVB or recurrence with distant metastases disease. The data is extrapolated from the phase II DESTINY-PanTumor02 interim results. The study looked at 267 patients with solid state tumors that had HER2 expression and had prior HER2 targeted therapy. ORR was 37.1% with a median DOR of 11.8 months. Safety results showed AEs of Grade (G) >=3 occurred in 58.4% of patients, while 11.6% discontinued due to treatment adverse events. 18 patients had drug-related interstitial lung disease/pneumonitis.

NCCN also provides a category 2A recommendation in head and neck cancer—salivary gland tumor. NCCN notes that Enhertu is useful in certain circumstances as a single-agent in systemic therapy for HER2-positive recurrent disease. The evidence cited comes from a retrospective analysis of two phase 1 trials within clinicaltrials.gov that are ongoing and have yet to be published. The analysis showed Enhertu provided an overall response of 47% (8/17) and the best overall response was PR in 8 patients and SD in 9 patients. Median duration of response and PFS were 12.9 months and 14.1 months, respectively. The most common grade 3 or 4 adverse events were neutropenia, decreased white blood cell count, and anemia.

NCCN also provides a category 2A recommendation for multiple solid-state tumors due to extrapolation of the FDA indication in solid tumors. These can include (but not all encompassing) Ampullary adenocarcinoma, Biliary Tract Cancers, Bladder Cancer, Cervical, Colorectal Cancer, Endometrial Cancer, Head and Neck Cancers including Salivary Gland Tumors, Non-Small Cell Lung Cancer, Ovarian Cancer, Pancreatic Cancer, Small Bowel Adenocarcinoma, Uterine, Vaginal or Vulvar Cancer.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

Definitions and Measures

- HER2 testing (adapted from American Society of Clinical Oncology/College of American Pathologists):
- Positive HER2:
  - IHC 3+ based on circumferential membrane staining that is complete, intense. (Observed in a homogeneous and contiguous population and within > 10% of the invasive tumor cells).
  - ISH positive based on:
    - Single-probe average HER2 copy number ≥ 6.0 signals/cell*
    - Dual-probe HER2/CEP 17 ratio ≥ 2.0* with an average HER2 copy number ≥ 4.0 signals/cell
    - Dual-probe HER2/CEP17 ratio ≥ 2.0* with an average HER2 copy number < 4.0 signals/cell
    - Dual-probe HER2/CEP17 ratio < 2.0* with an average HER2 copy number ≥ 6.0 signals/cell

  *(Observed in a homogeneous and contiguous population and within >10% of the invasive tumor cells. By counting at least 20 cells within the area)
- Equivocal HER2:
  - IHC 2+ based on circumferential membrane staining that is incomplete and/or weak/moderate and within >10% of the invasive tumor cells or complete and circumferential membrane staining that is intense and within ≤10% of the invasive tumor cells.
  - ISH equivocal based on:
    - Single-probe average HER2 copy number ≥ 4.0 and < 6.0 signals/cell
    - Dual-probe HER2/CEP17 ratio < 2.0 with an average HER2 copy number ≥ 4.0 signals/cell
- Negative HER2 if a single test (or both tests) performed show:
  - IHC 1+ as defined by incomplete membrane staining that is faint/barely perceptible and within > 10% of the invasive tumor cells
  - IHC 0 as defined by no staining observed or membrane staining that is incomplete and is faint/barely perceptible and within ≤ 10% of the invasive tumor cells
  - ISH negative based on:
    - Single-probe average HER2 copy number < 4.0 signals/cell
    - Dual-probe HER2/CEP17 ratio < 2.0 with an average HER2 copy number < 4.0 signals/cell
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.
- Progressive Disease (PD): Cancer that is growing, spreading, or getting worse.
- Refractory Disease: Illness or disease that does not respond to treatment.
- Targeted biologic agent: A newer type of drug developed specifically to target genetic changes in cells that cause cancer. It works differently than standard chemotherapy drugs, often with different side effects.
- Unresectable: Unable to be removed with surgery.

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			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

Approved Indications

A. Breast cancer, unresectable or metastatic, hormone receptor positive, HER2 low or HER2 ultralow
   a. Breast cancer, unresectable or metastatic, HER2 low (previously treated)
B. Breast cancer, unresectable or metastatic, HER2 positive
   a. In combination with pertuzumab as first-line for unresectable/metastatic HER2+ (IHC 3+ or ISH+) breast cancer; and
   b. As monotherapy for unresectable/metastatic HER2+ (IHC 3+ or ISH+) breast cancer after prior anti-HER2 regimen (metastatic, or recurrence during/within 6 months of completing neoadjuvant/adjuvant therapy).
C. Gastric cancer, locally advanced or metastatic, HER2 positive (gastric or gastroesophageal junction adenocarcinoma; previously treated)
D. Non–small cell lung cancer, unresectable or metastatic, HER2 (ERBB2) mutation positive (previously treated)
E. Solid tumors, unresectable or metastatic, HER2 positive (IHC 3+) (previously treated)

Other Uses

A. See Background Information section above.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Fam-trastuzumab deruxtecan-nxki (Enhertu)	MP-RX-FP-180-26	☒ **MMM MA** ☒ **MMM MultiHealth**	03/23/2026	03/24/2026
			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Fam-trastuzumab deruxtecan-nxki (Enhertu®)

A. Criteria For Initial Approval

Requests for Enhertu (fam-trastuzumab deruxtecan-nxki) may be approved if the following criteria are met:

i. Individual has a diagnosis of recurrent unresectable or metastatic HER2-positive (HER2+) breast cancer (NCCN 1, 2A) and meets one of the following HER2 levels:
   A. Immunohistochemistry (IHC) is 3 +; **OR**
   B. In situ hybridization (ISH) positive; **AND**

ii. Individual has previously received a prior anti-HER2 therapy in either:
   A. Metastatic setting; **OR**
   B. In the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy;

OR

iii. Individual has a diagnosis of unresectable or metastatic HER2-Low breast cancer and meets one of the following HER2 levels (Label, NCCN 1, 2A):
   A. IHC is 1+; **OR**
   B. IHC is 2+/ISH negative; **AND**

iv. Individual is using as a single agent; **AND**

v. Individual is using in one of the following ways:
   A. Individual has progressed on one or more endocrine therapies in the metastatic setting; **OR**
   B. Individual has prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy;

OR

vi. Individual has a diagnosis of unresectable or metastatic HER2-Ultralow breast cancer (Label); **AND**
   A. Individual has IHC 0 with member straining; **AND**
   B. Individual is using as a single agent; **AND**
   C. Individual has progressed on one or more endocrine therapies in the metastatic setting;

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Fam-trastuzumab deruxtecan-nxki (Enhertu)	MP-RX-FP-180-26	☒ **MMM MA** ☒ **MMM MultiHealth**	03/23/2026	03/24/2026
			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

OR

vii. Individual has a diagnosis of HER2-positive cervical cancer, including vaginal cancer (NCCN 2A); **AND**
- A. Individual meets one of the following HER2 levels:
  1. IHC 3+ ; **OR**
  2. IHC 2+; **AND**
- B. Individual is using as second-line or subsequent therapy; **AND**
- C. Individual is using as a single agent; **AND**
- D. Using in one of the following disease states:
  1. Local/regional recurrence; **OR**
  2. Stage IVB or recurrence with distant metastases;

OR

viii. Individual has a diagnosis of colorectal cancer (including appendiceal adenocarcinoma) (NCCN 2A); **AND**
- A. Individual is using as initial treatment; **AND**
  - A. Individual is using as a single agent; **AND**
  - B. Individual has HER2-amplified (defined as IHC 3+ or ISH positive) and RAS and BRAF wild-type disease; **AND**
  - C. Individual has unresectable metachronous metastases pMMR/MSS only and previous FOLFOX or CapeOX treatment within the past 12 months;

OR

- B. Individual is using as subsequent therapy; **AND**
  - A. Individual is using as a single agent; **AND**
  - B. Using in one of the following disease states:
    - a. Individual has advanced disease; **OR**
    - b. Individual has metastatic disease which is proficient mismatch repair/microsatellite-stable (pMMR/MSS) or ineligible for or progression on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta [POLE/POLD1] mutation who are HER2-amplified (defined as IHC 3+ or ISH positive) and RAS and BRAF wild-type; **OR**
    - c. Adjuvant treatment for unresectable metachronous metastases that converted to resectable disease after initial treatment;

ix. Individual has a diagnosis of HER2-Positive disease in solid tumors (Label, NCCN 2A); AND
- A. Individual has HER2 levels of IHC 3+; **AND**
- B. Individual has an unresectable or metastatic solid tumor; **AND**
- C. Individual has had prior systemic treatment; **AND**
- D. Individual has no satisfactory alternative treatment options; **AND**
- E. Individual is using as a single agent;

OR

Policy Name: Fam-trastuzumab deruxtecan-nxki (Enhertu)	Policy Number: MP-RX-FP-180-26	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 03/23/2026	Effective Date: 03/24/2026
			Last Review Date: 03/24/2026	Frequently Revision: Annual

x. Individual has a diagnosis of unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations and who have received a prior systemic therapy (Label, NCCN 2A);

OR

xi. Individual has a diagnosis of locally advanced or metastatic HER2+ gastric or esophageal and esophagogastric junction cancers and meets one of the following HER2 levels (Label, NCCN 2A):
   A. Individual meets one of the following HER2 levels:
      1. IHC 3 +; **OR**
      2. IHC 2+ /ISH positive; **AND**
   B. Individual has had received a prior trastuzumab (or trastuzumab biosimilars)-based regimen;

xii. Individual has a diagnosis of HER2-positive endometrial carcinoma (NCCN 2A); **AND**
   A. Individual meets one of the following HER2 levels:
      A. IHC 3+; **OR**
      B. IHC 2+; **AND**
   B. Individual is using as second-line or subsequent therapy; AND C. Individual is using for recurrent disease;

xiii. Individual has a diagnosis of metastatic HER2 + breast cancer with brain metastases and the following criteria are met (NCCN 2A):
   A. Individual has a primary diagnosis of HER2+ breast cancer; **AND**
   B. Using in one of the following ways:
      A. In those with asymptomatic brain metastases as primary or initial therapy; **OR**
      B. In those with stable brain metastases disease in relapsed/recurrent disease; **AND**
   C. Individual is using as a single-agent treatment.

OR

xiv. Individual has a diagnosis of HER2+ unresectable/metastatic breast cancer and the following criteria are met:
   A. Individual is an adult with unresectable or metastatic HER2+ breast cancer (IHC 3+ or ISH+), as determined by an FDA-approved test; **AND**
   B. Enhertu (fam-trastuzumab deruxtecan-nxki) is used as first-line treatment; **AND**
   C. Enhertu (fam-trastuzumab deruxtecan-nxki) is used in combination with pertuzumab;

   OR

xv. Individual has a diagnosis of unresectable or metastatic HER2-positive (IHC 3+ or ISH+) breast cancer; **AND**
   A. Individual is an adult with HER2-positive status as determined by an FDA-approved test; **AND**
   B. Enhertu is used as monotherapy; **AND**

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

C. Individual has received a prior anti-HER2-based regimen in either:
   a. Metastatic setting; **OR**
   b. Neoadjuvant/adjuvant setting with disease recurrence during or within 6 months of completing therapy.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Enhertu (fam-trastuzumab deruxtecan-nxki) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:

   A. Individual continues to meet the applicable Criteria for Initial Approval in Section A for the requested diagnosis/indication; **AND**
   B. Documentation is provided that the individual has experienced a clinical response or clinical benefit (for example, objective response, stable disease, improvement in disease-related symptoms, or no evidence of disease progression); **AND**
   C. Documentation is provided that the individual has no evidence of unacceptable toxicity and is able to continue therapy per prescribing information, including monitoring and management consistent with boxed warnings for interstitial lung disease (ILD)/pneumonitis (including fatal cases) and embryo-fetal toxicity.

C. Conditions not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Requests for Enhertu (fam-trastuzumab deruxtecan-nxki) may not be approved for the following:

i. When Enhertu is used in combination with other targeted biologic agents or chemotherapy agents; **OR**
ii. Individual has a history of Interstitial Lung Disease (ILD)/pneumonitis requiring treatment with steroids or ongoing ILD/pneumonitis; **OR**
iii. When the above criteria are not met and for all other indications.

D. Authorization Duration

i. Initial Approval Duration: 6 months
ii. Reauthorization Approval Duration: 6 months

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Fam-trastuzumab deruxtecan-nxki (Enhertu)	MP-RX-FP-180-26	☒ **MMM MA** ☒ **MMM MultiHealth**	03/23/2026	03/24/2026
			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Indication	
Enhertu® (fam-trastuzumab deruxtecan-nxki) for injection 100 mg SDV	• HER2+ mBC *(in combination with pertuzumab)* • HER2-low or HER2-ultralow mBC • HER2-mutant mNSCLC • HER2+ (IHC 3+) metastatic solid tumors	• 5.4 mg/kg IV every 3 weeks until disease progression or unacceptable toxicity.
	• HER2+ aGC	• 6.4 mg/kg every 3 weeks until disease progression or unacceptable toxicity.
Exceptions		
• ENHERTU should not be substituted for or with trastuzumab or ado-trastuzumab emtansine. • Management of adverse reactions (ILD, neutropenia, thrombocytopenia, or left ventricular dysfunction) may require temporary interruption, dose reduction, or discontinuation of ENHERTU. See package insert for additional information.		

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Fam-trastuzumab deruxtecan-nxki (Enhertu)	MP-RX-FP-180-26	☒ **MMM MA** ☒ **MMM MultiHealth**	03/23/2026	03/24/2026
			Last Review Date: 03/24/2026	**Frequently Revision:** Annual

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
C15.3–C15.9	Malignant neoplasm of the esophagus
C16.0–C16.9	Malignant neoplasm of stomach
C18.0–C18.9	Malignant neoplasm of colon
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–C34.92	Malignant neoplasm of bronchus and lung
C50.011–C50.929	Malignant neoplasm of the breast
C52	Malignant neoplasm of vagina
C53.0–C53.9	Malignant neoplasm of cervix uteri
C54.0–C54.9	Malignant neoplasm of corpus uteri
C55	Malignant neoplasm of uterus, part unspecified
C77.0–C77.9	Secondary and unspecified malignant neoplasm of lymph nodes
C78.00–C78.39	Secondary malignant neoplasm of lung and pleura
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31–C79.32	Secondary malignant neoplasm of brain and cerebral meninges
Z17.31	Human epidermal growth factor 2 positive status [HER2+]
Z85.3	Personal history of malignant neoplasm of breast

HCPCS Codes:

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

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Fam-trastuzumab deruxtecan-nxki (Enhertu)	MP-RX-FP-180-26	☒ **MMM MA** ☒ **MMM MultiHealth**	03/23/2026 **Last Review Date:** 03/24/2026	03/24/2026 **Frequently Revision:** Annual

Reference Information:

1. Cortés J, Kim S-B, Chung W-P, et al. Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients with HER2+ metastatic breast cancer: results of the randomized, phase 3 study DESTINY-Breast03. ESMO 2021
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Jerusalem G, Park YH, Yamashita T, et al. Trastuzumab deruxtecan (T-DXd) in patients with HER2+ metastatic breast cancer with brain metastases: a subgroup analysis of the DESTINY-Breast01 trial. ASCO 2021
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
6. Li BT, et al. Trastuzumab deruxtecan in HER2-mutant non-small-cell lung cancer. N Engl J Med 2022;386:241-251.
7. Modi S, Saura C, Yamashita T, et al. Trastuzumab Deruxtecan in Previously Treated HER2-Positive breast Cancer. N Eng J Med 2019: 10.1056/NEJMoa1914510.
8. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 17, 2025.
    a. Breast Cancer. V1.2026. Revised January 16, 2026.
    b. Central Nervous System Cancers V2.2026. Revised December 5, 2025.
    c. Cervical Cancer. V1.2025. Revised November 10, 2025.
    d. Colon Cancer V6.2024. Revised January 17, 2025.
    e. Esophageal and esophagogastric junction cancers. V5.2024. Revised December 20, 2024.
    f. Gastric Cancer. V2.2023. Revised August 29, 2023.
    g. Head and neck cancers. V1.2025. Revised November 26, 2024
    h. Non-Small Cell Lung Cancer. V3.2025. Revised January 14, 2025.
    i. Rectal Cancer V4.2024. Revised August 22, 2024.
    j. Uterine neoplasms. V1.2025. Revised December 16, 2024.
9. Siena S, Di Bartolomeo M, Raghav K, et al. Trastuzumab deruxtecan (DS-8201) in patients with HER2-expressing metastatic colorectal cancer (DESTINY-CRC01): a multicentre, open-label, phase 2 trial. Lancet Oncol 2021;22:779-789.
10. Smit EF, Nakagawa K, Nagasaka M, et.al. Trastuzumab deruxtecan in patients with HER2-mutated metastatic non-small cell lung cancer; interim results of DESTINY-Lung01[abstract]. J Clin Oncol 2020;38; Abstract 9504.
11. Curigliano G, et al. Trastuzumab deruxtecan (T-DXd) vs. physician's choice of chemotherapy (TPC) in patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-low or HER2-ultralow metastatic breast cancer (mBC) with prior endocrine therapy (ET): Primary results from DESTINY-Breast06 (DB-06). J Clin Oncol 42(suppl 17): LBA1000. doi: 10.1200/JCO.2024.42.17_suppl.LBA1000
12. Daiichi Sankyo, Inc. (2025). *Enhertu (fam-trastuzumab deruxtecan-nxki) for injection, for intravenous use* [Prescribing information] (Revised 12/2025). Retrieved February 14, 2026,

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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from https://daiichisankyo.us/prescribing-information-portlet/getPIContent?productName=Enhertu&inline=true

13. UpToDate, Inc. (n.d.). *Fam-trastuzumab deruxtecan: Drug information*. In *UpToDate*. Retrieved February 14, 2026, from https://www.uptodate.com/contents/fam-trastuzumab-deruxtecan-drug-information?search=enhertu&source=panel_search_result&selectedTitle=1~26&usage_type=panel&kp_tab=drug_general&display_rank=1#F53966097

Federal and state laws or requirements, contract language, and Plan utilization management progr polices may take precedence over the application of this clinical criteria.

Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption. Added new indication and criteria for Initial Approval for First-Line Treatment of Patients with HER2-Positive Metastatic Breast Cancer. Added Continuation of Therapy criteria and a dosing/quantity limitations table. Coding reviewed: added ICD10 codes C15.0-C15.2. Updated reference list. Administrative update to change policy template.	3/17/2026	03/24/2026