

Generic Name: fam-trastuzumab deruxtecan-nxki

Therapeutic Class or Brand Name: Enhertu

Applicable Drugs: N/A

Preferred: N/A

Non-preferred: N/A

Date of Origin: N/A

Date Last Reviewed / Revised: 2/9/2026

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I to V are met.)

- I. Documentation of one of the following diagnoses A through D AND must meet all criteria listed under the applicable diagnosis:

FDA-Approved Indication(s)

A. Breast Cancer

- i. Documentation of unresectable or metastatic disease and meets one of the following (1, 2, OR 3):

1. Documentation of HER-2 positive (IHC 3+ or ISH+) disease as determined by an FDA-approved test and meets one of the following (a. OR b.):

- a. Enhertu will be used in combination with pertuzumab for first line treatment

- b. Enhertu will be used as monotherapy

- i. Documentation patient has received a prior anti-HER2-based regimen either in the metastatic setting, or, in the neoadjuvant or adjuvant setting and disease has recurred during or within six months of completing treatment

2. Documentation of hormone receptor positive (HR-positive), HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) disease, as determined by an FDA-approved test

- a. Documentation of progression on one or more endocrine therapies for metastatic disease

- b. Enhertu will be used as monotherapy

3. Documentation of HER2-low (IHC 1+ or IHC 2+/ISH-) disease, as determined by an FDA-approved test

- a. Enhertu will be used as monotherapy and meets one of the following (i. OR ii.)

- i. Documentation of treatment with prior chemotherapy for metastatic disease

- ii. Documentation of disease recurrence during or within 6 months of completing adjuvant chemotherapy

B. Non-Small Cell Lung Cancer

- i. Documentation of unresectable or metastatic disease
- ii. Documentation of HER2 (ERBB2) tyrosine kinase domain (TKD) activating mutation as detected by an FDA-approved test
- iii. Documentation of progression on or intolerance to at least one prior systemic therapy
- iv. Enhertu will be used as monotherapy

C. Gastric Cancer or Gastroesophageal Junction Adenocarcinoma

- i. Documentation of locally advanced or metastatic disease
- ii. Documentation of HER2-positive (IHC 3+ or IHC 2+/ISH positive) disease, as detected by an FDA-approved test
- iii. Documentation of previous treatment with a trastuzumab-based regimen
- iv. Enhertu will be used as monotherapy

D. Solid Tumors

- i. Documentation of unresectable or metastatic solid tumor (ex: appendiceal cancer, biliary tract cancer, bladder cancer, colon cancer, head and neck cancer, ovarian cancer, pancreatic cancer, rectal cancer, etc.)
- ii. Documentation of HER2-positive (IHC 3+) disease as detected by an FDA-approved test
- iii. Documentation the patient has received prior systemic treatment and has no satisfactory alternative treatment options
- iv. Enhertu will be used as a single agent

II. Minimum age requirement: 18 years old

III. Treatment must be prescribed by or in consultation with an oncologist or hematologist.

IV. Request is for a medication with the appropriate FDA labeling, or its use is supported by current National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1 or 2A.

V. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- N/A

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Maximum dose based on weight and indication
 - Gastric cancer: 6.4 mg/kg every 21 days
 - All other FDA-approved indications: 5.4 mg/kg every 21 days
- Maximum day supply: once every 21 days

APPROVAL LENGTH

- **Authorization:** 6 months
- **Re-Authorization:** 6 months; An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and does not show evidence of progressive disease.

APPENDIX

N/A

REFERENCES

1. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. Version 2.2026. Updated December 2, 2025. Accessed December 4, 2025. www.nccn.org/professionals/physician_gls/pdf/NSLCL.pdf
2. Enhertu. Prescribing Information. Daiichi Sankyo, Inc. 2025. Accessed December, 2025. Daiichisankyo.us/prescribing-information-portlet/getPIContent?productName=Enhertu&inline=true
3. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Breast Cancer. Version 5.2025. Updated October 16, 2025. Accessed December 22, 2025. www.nccn.org/professionals/physician_gls/pdf/breast.pdf
4. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Gastric Cancer. Version 1.2026. Updated December 12, 2025. Accessed December 23, 2025. www.nccn.org/professionals/physician_gls/pdf/gastric.pdf
5. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Esophageal and Esophagogastric Junction Cancers. Version 1.2026. Updated December 10,

2025. Accessed December 23, 2025.

www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.