Clinical Policy: Fam-Trastuzumab Deruxtecan-nxki (Enhertu)

Reference Number: ERX.SPA.376
Effective Date: 03.01.20
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Fam-trastuzumab deruxtecan-nxki (Enhertu®) is a human epidermal growth factor receptor 2 (HER2)-directed antibody and topoisomerase inhibitor conjugate.

FDA Approved Indication(s)
Enhertu is indicated for the treatment of adult patients with:

- Unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2 based regimen either:
  - In the metastatic setting, or
  - In the neoadjuvant setting and have developed disease recurrence during or within six months of completing therapy.
- Locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (esophagogastric junction; EGJ) adenocarcinoma who have received a prior trastuzumab-based regimen

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

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Enhertu is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Diagnosis of recurrent, unresectable or metastatic HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of one prior anti-HER2-based regimens (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;
   b. Rapid disease progression within 6 months of neoadjuvant or adjuvant therapy (12 months for pertuzumab-containing regimens);

   **Prior authorization may be required for anti-HER2-based regimens*
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 5.4 mg/kg every 3 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Gastric and Esophagogastric Junction Cancer (must meet all)**:**

1. Diagnosis of HER2-positive gastric or EGJ adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;

4. Disease is locally advanced or metastatic;
5. Failure of trastuzumab-based regimen (*see Appendix B*);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 6.4 mg/kg every 3 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Cancer (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or documentation supports that member is currently receiving Enhertu for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For breast cancer: New dose does not exceed 5.4 mg/kg every 3 weeks;
   b. For gastric or EGJ adenocarcinoma: New dose does not exceed 6.4 mg/kg every 3 weeks;
   c. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
EGJ: esophagogastric junction
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
NCCN: National Comprehensive Center Network

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Breast Cancer NCCN examples of systemic therapies for HER2-positive recurrent or metastatic disease • Aromatase inhibitor ± trastuzumab • Aromatase inhibitor ± lapatinib • Pertuzumab + trastuzumab + docetaxel	Varies	Varies
Gastric and Esophagogastric Junction Cancer trastuzumab-based regimen	8 mg/kg IV q 3 weeks	8 mg/kg

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): none reported
- Boxed warning(s): interstitial lung disease and pneumonitis; embryo-fetal toxicity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	5.4 mg/kg IV every 3 weeks	5.4 mg/kg
Gastric cancer	6.4 mg/kg IV every 3 weeks	6.4 mg/kg

VI. Product Availability
Single-dose vial: 100 mg lyophilized powder

VII. References
1. Enhertu Prescribing Information. Basking Ridge, NJ: Daiichi Sankyo, Inc.; May 2022. Available at: www.enhertu.com. Accessed May 18, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed May 18, 2022.
3. National Comprehensive Cancer Network. Breast Cancer Version 2.2022. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed May 20, 2022.
4. Modi S, Saura C, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. *N Engl J Med*. 2019; doi: 10.1056/NEJMoa1914510.
5. National Comprehensive Cancer Network. Gastric Cancer Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed May 18, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.14.20	02.20
1Q 2021 annual review: recurrent breast cancer added per NCCN; RT4: added criteria for new FDA-approved gastric cancer indication; therapeutic alternatives and references reviewed and updated.	10.13.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.13.21	02.22
RT4: added criteria for new FDA-approved indication as 2nd line for breast cancer; added criteria for 1st-line therapy for breast cancer in select patients per NCCN; references reviewed and updated.	05.18.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.