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

Reference Number: CP.PHAR.456
Effective Date: 03.01.20
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.

It is the policy of health plans affiliated with Centene Corporation® 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cancer (must meet all)**:**
1. Currently receiving medication via Centene benefit, 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 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:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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 for all relevant lines of business 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	6.4 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 ww.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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9358	Injection, fam-trastuzumab deruxtecan-nxki, 1 mg

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; updated coding implications; therapeutic alternatives and references reviewed and updated; references to HIM.PHAR.21 revised to HIM.PA.154.	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 per PI; added criteria for 1st-line therapy for breast cancer in select patients per NCCN; referenes 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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.