Drug Policy:

Enhertu™ (fam-trastuzumab deruxtecan-nxki)

POLICY NUMBER UM ONC_1379	**SUBJECT** Enhertu™ (fam-trastuzumab deruxtecan-nxki)	**DEPT/PROGRAM** UM Dept	**PAGE 1 of 4**
DATES COMMITTEE REVIEWED 02/12/20, 08/12/20, 12/09/20, 11/10/21, 03/09/22, 05/11/22, 06/08/22, 09/14/22, 11/09/22, 11/08/23, 05/08/24	**APPROVAL DATE** May 08, 2024	**EFFECTIVE DATE** May 31, 2024	**COMMITTEE APPROVAL DATES** 02/12/20, 08/12/20, 12/09/20, 11/10/21, 03/09/22, 05/11/22, 06/08/22, 09/14/22, 11/09/22, 11/08/23, 05/08/24
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee	
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**	**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Enhertu (fam-trastuzumab deruxtecan-nxki) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. HER-2 positive metastatic/recurrent Breast Cancer

1. The member has recurrent or metastatic HER2 positive breast cancer AND Enhertu (fam-trastuzumab deruxtecan-nxki) will be used as monotherapy for any of the following clinical settings:

a. As first line therapy, for recurrent/metastatic disease, in a member who has experienced disease progression within 6 months of neoadjuvant/adjuvant treatment or within 12 months of extended adjuvant treatment with an anti-HER2 containing regimen [e.g., Herceptin (trastuzumab)/trastuzumab biosimilar +/- Perjeta (pertuzumab) +/- chemotherapy.

b. As second line/subsequent therapy in the metastatic setting.

C. HER-2 LOW Metastatic Breast Cancer

1. Enhertu may be used as a single agent in metastatic HER-2 LOW breast cancer. HER-2 LOW is defined as one of the following: HER-2 IHC staining 2+ with a negative ISH/FISH, or HER-2 by IHC of 1+ (in which case FISH/ISH is not required); the above definition is regardless of Hormone Receptor status. Member should have received one or more lines of systemic chemotherapy for metastatic breast cancer excluding hormonal agents [for example Faslodex (fulvestrant) or CDK 4/6 inhibitors [e.g., Ibrance (Palbociclib), Kisqali (ribociclib), Verzenio (abemaciclib)].

D. HER-2 Positive, Metastatic/Recurrent Gastric, Esophageal and GE Junction Adenocarcinoma

1. The member has metastatic/recurrent, HER-2 positive Gastric, Esophageal or GE Junction adenocarcinoma AND
2. The member has experienced disease progression on a prior regimen that included trastuzumab/trastuzumab biosimilar AND
3. Enhertu (fam-trastuzumab deruxtecan-nxki) will be used as a single agent.

E. Non-Small Cell Lung Cancer (NSCLC)

1. The member has unresectable or metastatic Non-Small Cell Lung Cancer with an activating ERBB-2/HER-2 mutation and Enhertu (fam-trastuzumab deruxtecan-nxki) may be used following at least one prior systemic therapy.

F. Solid Tumors

1. Enhertu (fam-trastuzumab deruxtecan-nxki) may be used in adult members with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.

III. EXCLUSION CRITERIA

A. Enhertu (fam-trastuzumab deruxtecan-nxki) is being used during or after disease progression with the same regimen.

B. For HER-2 positive Gastric, Esophageal and GE Junction adenocarcinoma: Use of Enhertu (fam-trastuzumab deruxtecan-nxki) without receiving prior trastuzumab treatment.

C. Members with HER-2 protein overexpression as determined by IHC and members with HER-2 gene amplification (Rationale: Only patients with activating HER-2 mutations were enrolled in the published trial DESTINY 01 Lung trial that led to FDA approval; the trial is referenced below).

D. Dosing exceeds single dose limit of Enhertu (fam-trastuzumab deruxtecan-nxki) 5.4 mg/kg (for breast cancer and NSCLC) and 6.4 mg/kg (for gastric, esophageal, or GE junction cancer).

E. Investigational use of Enhertu (fam-trastuzumab deruxtecan-nxki) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is

not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

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K. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2023.

L. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

M. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

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