Reference number(s)
3470-A

SPECIALTY GUIDELINE MANAGEMENT

ENHERTU (fam-trastuzumab deruxtecan-nxki)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. HER2-positive Breast Cancer
   Enhertu is indicated for the treatment of adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer who have received a prior anti-HER2 based regimen either:
   i. in the metastatic setting, or
   ii. in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy.
2. HER2-low Breast Cancer
   Enhertu is indicated for the treatment of adult patients with unresectable or metastatic HER2-low [immunohistochemistry score (IHC) 1+ or IHC 2+/ in situ hybridization test (ISH) negative] breast cancer, as determined by an FDA-approved test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.
3. Gastric or Gastroesophageal Junction Adenocarcinoma
   Enhertu is indicated for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.
4. Non-Small Cell Lung Cancer (NSCLC)
   Enhertu is indicated for the treatment of adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.

B. Compendial Uses
1. HER2-positive breast cancer, treatment of recurrent disease
2. HER2-low breast cancer, treatment of recurrent disease
3. Non-small cell lung cancer with HER2 mutations, treatment of recurrent and advanced disease
4. HER2-amplified and RAS and BRAF wild-type colorectal cancer (including appendiceal and anal adenocarcinoma)
5. HER2-positive esophageal cancer
6. HER2-positive cervical cancer
7. HER2-positive endometrial carcinoma
8. HER2-positive salivary gland tumor

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: human epidermal growth factor receptor 2 (HER2) status (e.g., immunohistochemistry (IHC) score, in situ hybridization (ISH) test), RAS mutation status (where applicable), BRAF mutation status (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer

Authorization of 12 months may be granted for treatment of breast cancer when either of the following criteria are met:

1. Member has HER2-positive breast cancer and meets all of the following criteria:
   i. The disease had no response to preoperative systemic therapy, or the disease is recurrent, metastatic, or unresectable
   ii. The requested medication will be used as a single agent.
2. Member has HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer and meets all of the following criteria:
   i. The disease had no response to preoperative systemic therapy, or the disease is recurrent, metastatic or unresectable
   ii. The member has tried at least one prior chemotherapy in the metastatic setting or developed recurrence during or within 6 months of completing adjuvant chemotherapy
   iii. The requested medication will be used as a single agent

B. Non-small cell lung cancer

Authorization of 12 months may be granted for subsequent treatment of non-small cell lung cancer with HER2 (ERBB2) mutations when both of the following criteria are met:

1. The disease is recurrent, advanced, metastatic or unresectable
2. The requested medication will be used as a single agent

C. Colorectal Cancer

Authorization of 12 months may be granted for treatment of colorectal cancer (including appendiceal and anal adenocarcinoma) with HER2-amplified and RAS and BRAF wild-type disease as a single agent when the requested medication will be used as subsequent therapy for progression of advanced or metastatic disease.

D. Esophageal, Gastric or Gastroesophageal Junction Adenocarcinoma

Authorization of 12 months may be granted for subsequent treatment of HER2-positive locally advanced, recurrent or metastatic esophageal, gastric or gastroesophageal junction adenocarcinoma as a single agent.

E. Cervical Cancer

Authorization of 12 months may be granted for subsequent treatment of recurrent or metastatic HER2-positive (IHC 3+ or 2+) cervical cancer when used as a single agent.

F. Endometrial Carcinoma

Authorization of 12 months may be granted for subsequent treatment of recurrent HER2-positive (IHC 3+ or 2+) endometrial carcinoma when used as a single agent.

G. Salivary Gland Tumor

Authorization of 12 months may be granted for treatment of recurrent HER2-positive salivary gland tumor when used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Enhertu [package insert]. Basking Ridge, NJ: Daiichi Sankyo Inc.; August 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed October 10, 2023.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Anal Carcinoma. Version 2.2022. Accessed December 12, 2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf