PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Injectable) – Enhertu Prior Authorization Policy
- Enhertu® (fam-trastuzumab deruxtecan-nxki intravenous infusion – Daiichi Sankyo and AstraZeneca)

REVIEW DATE: 02/02/2022; selected revision 08/03/2022 and 08/17/2022

OVERVIEW

Enhertu is a human epidermal growth factor receptor 2 (HER2)-directed antibody and topoisomerase inhibitor conjugate indicated for the following uses:[1]

- **Breast cancer**
  - Treatment of adults with unresectable or metastatic HER2-positive disease who have received a prior anti-HER2-based regimen either in the metastatic setting or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy;
  - Treatment of adults with unresectable or metastatic HER2-low (immunohistochemistry [IHC] 1+ or IHC 2+/ in situ hybridization [ISH] negative) breast cancer who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.
- **Gastric cancer**, treatment of adults with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma, who have received a prior trastuzumab-based regimen.
- **Non-small cell lung cancer,** treatment of adults with unresectable or metastatic disease whose tumors have an activating HER2 (erb-b2 receptor tyrosine kinase 2 [ERBB2]) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.
- Enhertu cannot be substituted for or with trastuzumab or Kadcyla® (ado-trastuzumab emtansine intravenous infusion).

Guidelines

Enhertu is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **Breast Cancer:** NCCN guidelines (version 4.2022 – June 21, 2022) recommend Enhertu as a preferred second-line therapy regimen for the treatment of recurrent, unresectable (local or regional), or Stage IV metastatic disease that is HER2-positive (category 1).[2,3] The guidelines note that Enhertu may be considered in the first-line setting as an option for select patients (i.e. those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for Perjeta® {pertuzumab intravenous infusion}-containing regimens]) (category 2A). The guidelines note that Enhertu can be used for third-line therapy and beyond as well (category 2A). The guidelines recommend Enhertu as a preferred single-agent for recurrent unresectable (local or regional) or stage IV (M1) HER2 IHC 1+, or 2+ and ISH negative disease, in patients who have received at least one prior line of chemotherapy in the metastatic setting that is hormone receptor (HR) negative or HR positive and endocrine therapy refractory (category 1).
- **Colon or Rectal Cancer:** NCCN guidelines (version 1.2022 – February 25, 2022) supports use of Enhertu for colon and rectal cancer for patients in the first-line setting who are not candidates for intensive therapy or as subsequent therapy for HER-2 amplified and *RAS* and *BRAF* wild-type disease.[2,4,5]
- **Esophageal and Esophagogastric Junction Cancers**: NCCN guidelines (version 1.2022 – December 21, 2021) recommend Enhertu as a preferred regimen for second-line or subsequent

therapy for unresectable locally advanced, recurrent, or metastatic disease (where local therapy is not indicated) for HER2 overexpression positive adenocarcinoma (category 2A).[6]

- **Gastric Cancer:** NCCN guidelines (version 2.2022 – January 11, 2022) recommend Enhertu as a preferred regimen for second-line or subsequent therapy for unresectable locally advanced, recurrent, or metastatic disease (where local therapy is not indicated) for HER2 overexpression positive adenocarcinoma (category 2A).[7] Trastuzumab is recommended as a preferred regimen in addition to first-line chemotherapy (fluorouracil or capecitabine + oxaliplatin [category 2A] or cisplatin [category 1]) in HER2 overexpression positive adenocarcinoma.
- **Non-Small Cell Lung Cancer:** NCCN guidelines (version 1.2022 – December 7, 2021) support use of Enhertu for erb-b2 receptor tyrosine kinase 2 (ERBB2) or HER2 mutations.[2,8]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Enhertu. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Enhertu as well as the monitoring required for adverse events and long-term efficacy, approval requires Enhertu to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Enhertu is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Breast Cancer**. Approve for 1 year if the patient meets ALL of the following criteria (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has recurrent or metastatic breast cancer; AND
   - **C)** Patient meets one of the following criteria (i or ii):
     - **i.** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; OR
     - **ii.** Patient has HER2-low disease as shown by HER2 immunohistochemistry (IHC) 1+, or IHC 2+ and in situ hybridization (ISH) negative disease and meets one of the following criteria (a or b):
       - **a)** Patient has hormone receptor (HR) positive disease and is refractory to endocrine therapy; OR
       - **b)** Patient has HR negative disease; AND
   - **D)** Patient has tried at least one prior regimen; AND
   - **E)** The medication is prescribed by or in consultation with an oncologist.

2. **Gastric or Gastroesophageal Junction Cancer.** Approve for 1 year if the patient meets ALL of the following criteria (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
   - **C)** Patient has received at least one prior trastuzumab-based regimen; AND
   - **D)** The medication is prescribed by or in consultation with an oncologist.

3. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following criteria (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has unresectable or metastatic disease; AND
   - **C)** The disease has activating human epidermal growth factor receptor 2 (HER2) mutations; AND
   - **D)** Patient has tried at least one prior systemic therapy; AND
   - **E)** The medication is prescribed by or in consultation with an oncologist.

Other Uses with Supportive Evidence

4. **Colon or Rectal Cancer.** Approve for 1 year if the patient meets ALL of the following criteria (A, B, C, D, E, and F):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has unresectable, advanced, or metastatic disease; AND
   - **C)** Patient has human epidermal growth factor receptor 2 (HER2)-amplified disease; AND
   - **D)** Patient has wild-type *RAS* and *BRAF* disease; AND
   - **E)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has tried at least one chemotherapy; OR
       Note: Examples of chemotherapy are fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).
     - **ii.** Patient is not a candidate for intensive therapy, according to the prescriber; AND
   - **F)** The medication is prescribed by or in consultation with an oncologist.

5. **Esophageal Cancer.** Approve for 1 year if the patient meets ALL of the following criteria (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
   - **C)** Patient has received at least one prior trastuzumab-based regimen; AND
   - **D)** The medication is prescribed by or in consultation with an oncologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Enhertu is not recommended in the following situations.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Enhertu® intravenous infusion [prescribing information]. Basking Ridge, NJ and Wilmington, DE: Daiichi Sankyo and AstraZeneca; August 2022.
2. The NCCN Drugs & Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2022. Search term: fam-trastuzumab deruxtecan-nxki.
3. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 4.2022 – June 21, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 2, 2022.
4. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 3.2021 – September 10, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2022.
5. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 2.2021 – September 10, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2022.
6. The NCCN Esophageal and Esophagogastric Junction Cancers Clinical Practice Guidelines in Oncology (version 1.2022 – December 21, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 24, 2022.

7. The NCCN Gastric Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – January 11, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 24, 2022.
8. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2022 – March 16, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 15, 2022.