Fam-Trastuzumab Deruxtecan-nxki (Enhertu®)

NDC CODE(S) 65597-0406-XX ENHERTU 100MG Solution Reconstituted (SANKYO)

DESCRIPTION

Fam-trastuzumab deruxtecan-nxki is a HER2-directed antibody and topoisomerase inhibitor conjugate or antibody-drug conjugate (ADC). It consists of three components, a humanized anti-HER2 IgG1 monoclonal antibody (mAb), covalently linked to a topoisomerase inhibitor via a tetrapeptide-based cleavable linker. Fam-trastuzumab is the humanized anti-HER2 IgG1 monoclonal antibody (mAb). Deruxtecan is the protease-cleavable maleimide tetrapeptide linker and the topoisomerase inhibitor, DXd, which is an exatecan derivative.

POLICY

- Fam-trastuzumab deruxtecan-nxki for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Breast Cancer
  - Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma
  - Colorectal Adenocarcinoma
  - Non-Small Cell Lung Cancer (NSCLC)

- Fam-trastuzumab deruxtecan-nxki for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient at least 18 years of age; **AND**

Universal Criteria

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease; **AND**
- Used as single agent therapy; **AND**
- Therapy will not be substituted with or for any trastuzumab-based formulation (i.e., trastuzumab [or trastuzumab biosimilar product], ado-trastuzumab emtansine, trastuzumab-hyaluronidase, pertuzumab/trastuzumab and hyaluronidase-zzxf, etc.); **AND**

Breast Cancer

- Patient has recurrent, unresectable, or metastatic disease; **AND**
- Patient has previously been treated with at least two (2) prior HER2-targeted therapies for metastatic disease

Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma

- Patient has locally advanced or metastatic disease; **AND**
- Patient has previously been treated with a trastuzumab-based regimen

Colorectal Adenocarcinoma

- Patient has RAS and BRAF wild-type (WT) disease; **AND**
  - Used as subsequent therapy for progression of advanced or metastatic disease after at least one prior line of treatment in the advanced or metastatic disease setting; **OR**
  - Patient is not appropriate for intensive therapy; **AND**
    - Used as initial systemic therapy for locally unresectable (or medically inoperable) or metastatic disease; **OR**
    - Used for unresectable or metastatic disease that remains unresectable after primary treatment; **OR**
    - Used for metastatic disease in patients who have received adjuvant FOLFOX or CapeOX more than 12 months ago OR who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy

Non-Small Cell Lung Cancer (NSCLC)

- Patient has metastatic disease

*HER2-positive overexpression criteria:

• Immunohistochemistry (IHC) assay 3+
• Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number ≥ 4.0 signals/cell
• Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following:
  ○ HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; **OR**
  ○ HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; **OR**
  ○ HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: left ventricular dysfunction/symptomatic congestive heart failure, pulmonary toxicity (i.e., interstitial lung disease/pneumonitis), neutropenia/febrile neutropenia, etc.; **AND**
  - LVEF is > 45% and absolute decrease is ≤ 20% from baseline (LVEF results must be within the previous 3 months); **OR**
  - LVEF is 40% to 45% and absolute decrease is < 10% from baseline (LVEF results must be within the previous 3 months)

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Breast Cancer	Administer 5.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity

Gastric/Gastroesophageal Junction (GEJ) Adenocarcinoma	Administer 6.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
Colorectal Adenocarcinoma	Administer 6.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
Non-Small Cell Lung Cancer	Administer 6.4 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity

LENGTH OF AUTHORIZATION

Coverage will be provided for six months and may be renewed.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

- Breast Cancer: 600 billable units every 21 days
- All other indications: 700 billable units every 21 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Enhertu [package insert]. Basking Ridge, NJ; Daiichi Sankyo, Inc; January 202119. Accessed January2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) fam-trastuzumab deruxtecan. National Comprehensive Cancer Network, 20210. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January August 2021.

3. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 15.20210. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed January 2021.
5. Wolff AC, Hammond EH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol 2018;36:2105-2122.
6. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf.
7. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
8. Modi S, Saura C, Yamashita T, et al; DESTINY-Breast01 Investigators. Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer. N Engl J Med. 2019 Dec 11. Doi: 10.1056/NEJMoa1914510.
9. Shitara K, Bang YJ, Iwasa S, et al; DESTINY-Gastric01 Investigators. Trastuzumab Deruxtecan in Previously Treated HER2-Positive Gastric Cancer. N Engl J Med. 2020 Jun 18;382(25):2419-2430.
10. Siena S, Di Bartolomeo M, Raghav KPS, et al. A phase II, multicenter, open-label study of trastuzumab deruxtecan in patients with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01. J Clin Oncol 020;38(suppl; abstr 4000).
11. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer 1.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed January 2021.
12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer 1.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed January 2021.
13. Smit EF, Nakagawa K, Nagasaka M, et al. Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer (NSCLC): interim results of DESTINY-Lung01[abstract]. J Clin Oncol 2020;38:Abstract 9504.
14. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer 2.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the NationalLexicomp Online. (2021). Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed January 2021.
15. AHFS DI. *Fam-trastuzumab deruxtecan-nxki*. Retrieved February 11, 2021 from Lexicomp Online with AHFS.
16. MICROMEDEX Healthcare Series. Drugdex Evaluations. (2021, January). *Fam-trastuzumab deruxtecan-nxki*. Retrieved February 11, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 6/2/2021

ID_MRx