



Positive Quality Intervention: Fam-trastuzumab deruxtecan-nxki (Enhertu®) management

Description: Fam-trastuzumab deruxtecan-nxki is indicated for the treatment of:

- adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer previously treated with two or more anti-HER2-based regimens^{1,2}. This indication is under accelerated approval based on tumor response and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen^{1,6}

The purpose of this PQI is to provide guidance for management of fam-trastuzumab deruxtecan-nxki.

Background: Fam-trastuzumab deruxtecan-nxki is a HER2 directed antibody-drug conjugate (ADC). Fam-trastuzumab deruxtecan-nxki was FDA approved for metastatic breast cancer in December 2019 based on results from the DESTINY-Breast01 trial that established its efficacy and safety in patients previously treated with trastuzumab emtansine. The overall response (complete response and partial response) was 60.9%. Secondary endpoints included a median progression free survival of 16.4 months in all patients and 18.1 months in 24 patients enrolled with asymptomatic brain metastases.² Fam-trastuzumab deruxtecan-nxki was FDA approved in January 2021 for patients with gastric and gastroesophageal junction adenocarcinoma based on the results of the DESTINY-Gastric01 trial. This study evaluated the safety and efficacy versus physician's choice chemotherapy (irinotecan or paclitaxel monotherapy) in patients who had progressed on at least two prior regimens which included trastuzumab, a fluoropyrimidine and a platinum agent. The study demonstrated a statistically significant improvement in the major efficacy outcomes of median overall survival (12.5 vs 8.4 mo) and confirmed objective response rate (40.5% vs 11.3%). Additional efficacy outcomes of median progression free survival (5.6 vs 3.5 mo) and median duration of response (11.3 vs 3.9 mo) were also improved.⁶

PQI Process:

- Review the medical record
 - Ensure patient is an appropriate candidate for fam-trastuzumab deruxtecan-nxki (review indications)
 - Confirm patient does not have a history of Interstitial Lung Disease (ILD) and/or pneumonitis
 - Patients with this history were excluded from the DESTINY-Breast01 and DESTINY-Gastric01 studies. Although not a contraindication, ILD/pneumonitis is a boxed warning
 - Assess Left Ventricular Ejection Fraction (LVEF) prior to initiation
 - Patients with LVEF < 50% were not studied^{2,6}
 - Evaluate CBC prior to initiation, as well as prior to each dose, and as clinically indicated
- Review treatment plan
 - Verify premedication orders:
 - Antiemetics - Moderately emetogenic³- 5-HT3 antagonist + dexamethasone prior to treatment and consideration for days 2 and 3; PRN antiemetic available for home use

Important notice: National Community Oncology Dispensing Association, Inc. (NCODA), has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



PQI Process continued:

- Acetaminophen + H1 blocker may be included to prevent infusion related reactions per institutional policy or provider preference
- Verify dosing of fam-trastuzumab deruxtecan-nxki¹
 - Breast cancer dosing is 5.4 mg/kg intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
 - Gastric cancer dosing is 6.4 mg/kg intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
 - First infusion is administered over 90 minutes
 - If patient tolerates the first infusion, subsequent infusions may be given over 30 minutes
 - Slow or interrupt infusion rate if patient develops infusion-related symptoms
 - No dose adjustments required for mild or moderate renal or hepatic impairment
 - Patients with severe renal or hepatic impairment were not studied
- Monitoring¹
 - CBC: baseline, then before each treatment cycle
 - Fam-trastuzumab deruxtecan-nxki treatment should be interrupted for patients with a neutrophil count < 1,000 cells/mm³ or a platelet count < 50,000/microliter
 - Growth factor support may be used to maintain counts when appropriate^{2,5,6}
 - LVEF: baseline and at regular intervals during treatment as clinically indicated
 - Discontinue treatment if LVEF < 40%, if an absolute LVEF decrease of > 20% from baseline LVEF or symptomatic congestive heart failure
 - Interstitial lung disease (ILD) and pneumonitis: Monitor and promptly investigate signs and symptoms including cough, dyspnea, fever, and new or worsening respiratory symptoms.
 - Permanently discontinue in all patients with grade 2 or higher ILD/ pneumonitis, promptly initiate systemic corticosteroid treatment (e.g., ≥1 mg/kg/day prednisolone or equivalent). Continue upon improvement for at least 14 days followed by gradual taper (e.g., for at least 4 weeks)
 - See package insert for additional dose modifications and management information
 - Evaluate the need for dose modifications. Do not re-escalate dose after dose reduction is made
 - Dose modifications for breast cancer:
 - First dose reduction: 4.4 mg/kg
 - Second dose reduction: 3.2 mg/kg
 - Further required dose reductions: Discontinue treatment
 - Dose modifications for gastric cancer:
 - First dose reduction: 5.4 mg/kg
 - Second dose reduction: 4.4 mg/kg
 - Further required dose reductions: Discontinue treatment

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PQI Process continued:

- Preparation¹
 - Reconstitute fam-trastuzumab deruxtecan-nxki 100 mg vials with 5 mL of Sterile Water for Injection, USP for a final concentration of 20 mg/mL
 - Inject dose into a 100 mL bag of 5% Dextrose Injection, USP. Do not use sodium chloride
 - Fam-trastuzumab deruxtecan-nxki is compatible with an infusion bag made of polyvinylchloride, or polyolefin (copolymer of ethylene and polypropylene)
- Administration¹
 - IV over 30 – 90 minutes with an infusion set made of polyolefin or polybutadiene and a 0.2- or 0.22-micron in-line polyethersulfone or polysulfone filter
 - 5% dextrose is recommended for priming and flushing the administrative line
 - Cover the infusion bag to protect from light

Patient Centered Activities:

- Patient Education^{1,5}
 - Instruct patient to report any new or worsening shortness of breath, dry cough, wheezing, or fever
 - Caution patient regarding a decreased white blood cell count (the cells that fight infections)
 - Review the possibility this drug could weaken the pumping action of the heart muscle. Promptly report any chest pain or tightness, rapid weight gain, significant swelling in ankles or trouble breathing. Your physician will test your heart before starting treatment and during treatment to monitor
 - Remind patient that this drug may cause significant hair loss
 - Instruct patient to report adverse events including fever, diarrhea, nausea/vomiting or fatigue
 - Ensure patient has access to supportive medications
 - Anti-nausea: (5-HT3 receptor antagonist, metoclopramide, or prochlorperazine)
 - Anti-diarrheal: Loperamide
 - Provide written medication information to patient

Supplemental Information:

- Patient assistance: ENHERTU4U⁴
 - Patient Savings Program: Assists eligible commercial patients with their out-of-pocket costs
 - Patient Assistance Program: Assists qualifying uninsured, underinsured or Medicare patients who are having difficulty affording their medications
- Assistance may also be available through independent charitable patient assistance foundations

References:

1. Enhertu® (fam-trastuzumab deruxtecan-nxki) [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; January 2021.
2. Modi S, Saura C, Yamashita T, et al; DESTINY-Breast01 Investigators. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. *N Engl J Med* 2020;382(7):610-621.
3. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Antiemesis. Version 2.2020. April 23, 2020. Accessed October 12, 2020.
4. ENHERTU4U: Patent Access to Treatment. <https://www.enherthu4u.com/patient/affording-your-medicine.html>.
5. Fam-trastuzumab Deruxtecan-nxki (Enhertu®). JNCCN Spotlights: <https://jnccn360.org/breast/jnccn-spotlights/fam-trastuzumab-deruxtecan-nxki>. Accessed October 16, 2020.
6. Shitara K, Bang YJ, Iwasa S, et al. Trastuzumab Deruxtecan in Previously Treated HER2-Positive Gastric Cancer. *N Engl J Med* 2020; 382:2419-2430.

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