APPROVED IN TWO mBC INDICATIONS[1]

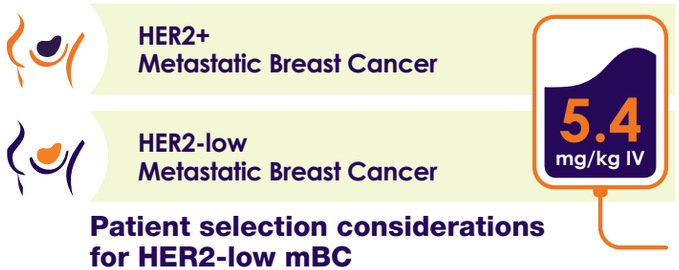
ENHERTU®
fam-trastuzumab deruxtecan-nxki
20 mg/mL INJECTION FOR INTRAVENOUS USE

PREPARATION AND ADMINISTRATION CONSIDERATIONS
for healthcare professionals

Recommended weight-based dosage and schedule[1]

ENHERTU is always given as a monotherapy

- ENHERTU mBC dosage **(5.4 mg/kg)** may differ from other approved indications



Patient selection considerations for HER2-low mBC

- Treat with ENHERTU based on HER2 expression (IHC 1+ or IHC 2+/ISH–)
- Information on FDA-approved tests for the detection of HER2 protein expression and HER2 gene amplification is available at: http://www.fda.gov/CcompanionDiagnostics

Continue until disease progression or unacceptable toxicity

Important Safety Information

Indications

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic:

- HER2-positive breast cancer 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
- HER2-low (IHC 1+ or IHC 2+/ISH-) 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

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

- **Interstitial lung disease (ILD) and pneumonitis, including fatal cases, have been reported with ENHERTU. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue ENHERTU in all patients with Grade 2 or higher ILD/pneumonitis. Advise patients of the risk and to immediately report symptoms.**
- **Exposure to ENHERTU during pregnancy can cause embryo-fetal harm. Advise patients of these risks and the need for effective contraception.**

Please see Important Safety Information throughout as well as on pages 6-8, and click here for full Prescribing Information, including Boxed WARNINGS, and click here for Medication Guide.

ENHERTU PREPARATION FOR ADMINISTRATION[1,2]

In order to prevent medication errors, check the vial labels to ensure that the drug being prepared and administered is ENHERTU® (fam-trastuzumab deruxtecan-nxki) and not trastuzumab or ado-trastuzumab emtansine.

Reconstitute and further dilute ENHERTU prior to intravenous infusion. Use appropriate aseptic technique.

ENHERTU is a hazardous drug. Follow applicable special handling and disposal procedures.

Before administering ENHERTU[1]

- Monitor complete blood counts prior to initiation and prior to each dose, and as clinically indicated
- Assess left ventricular ejection fraction (LVEF) prior to initiation and at regular intervals as clinically indicated
- Verify pregnancy status of females

How supplied, storage, and handling[1]

ENHERTU for injection is a white to yellowish white lyophilized powder supplied in 100 mg single-dose vials.

Prior to reconstitution
Store vials prior to reconstitution in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. **Do not freeze**. ENHERTU does not contain a preservative.

After reconstitution
If not used immediately, store the reconstituted ENHERTU vials in a refrigerator at 2°C to 8°C (36°F to 46°F) for up to 24 hours from the time of reconstitution and protected from light. **Do not freeze**. Discard unused portion after 24 hours refrigerated.

After dilution
If not used immediately, after dilution in IV bag with 5% Dextrose Injection, USP (D5W), store at room temperature for up to 4 hours including preparation and infusion, or in a refrigerator at 2°C to 8°C (36°F to 46°F) for up to 24 hours, protected from light. **Do not freeze**. Discard any unused portion left in the vial.

Do not shake the reconstituted or diluted solution.

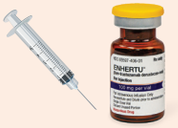
24-hour storage after dilution is permissible in addition to 24-hour storage following reconstitution[1]

Reconstitution[1]

Reconstitute immediately before dilution.

Calculate the dose (mg), the total volume of reconstituted ENHERTU solution required, and the number of vial(s) of ENHERTU needed.

Reconstitute each 100 mg vial by using a sterile syringe to slowly inject 5 mL of Sterile Water for Injection, USP into each vial to obtain a final concentration of 20 mg/mL.



Reconstitute only with Sterile Water for Injection, USP[1]

Swirl the vial gently until completely dissolved.
Do not shake.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The solution should be clear and colorless to light yellow. Do not use if visible particles are observed or if the solution is cloudy or discolored.

Dilution[1]

Dilution may occur immediately after or within 24 hours of reconstitution.

Dilute the calculated volume of reconstituted ENHERTU in an intravenous infusion bag containing **100 mL of D5W**. DO NOT use Sodium Chloride Injection, USP. ENHERTU is compatible with an infusion bag made of polyvinylchloride or polyolefin (copolymer of ethylene and polypropylene).

- **In clinical trials, dilution in 250 mL infusion bags of 5% dextrose with a drug concentration of 1 mg/mL to 6.7 mg/mL was permitted[3]**

⚠ **Dilute only with D5W[1]**

- **DO NOT use Sodium Chloride Solution, USP[1]**
- **Priming and flushing the administration line with D5W is recommended prior to administration of ENHERTU[3]**

Polyethylene and polypropylene are types of polyolefin[4]

Gently invert the infusion bag to thoroughly mix the solution. **Do not shake.**

Cover the infusion bag to protect from light.

A light protection cover should be used over the IV infusion bag containing diluted ENHERTU[1]

Discard any unused portion left in the vial.

Administration[1]

If the prepared infusion solution was stored refrigerated (2°C to 8°C [36°F to 46°F]), allow the solution to reach room temperature prior to administration protected from light. Cover the infusion bag to protect from light.

Administer ENHERTU as an intravenous infusion only with an infusion set made of polyolefin or polybutadiene.

Administer ENHERTU with a 0.20 or 0.22 micron in-line polyethersulfone (PES) or polysulfone (PS) filter.

Do NOT administer as an intravenous push or bolus.

Cover the infusion bag to protect from light during administration.

Do not mix ENHERTU with other drugs or administer other drugs through the same intravenous line.

First infusion: Administer infusion over 90 minutes.

Subsequent infusions: Administer over 30 minutes if prior infusions were well tolerated.

Polyethylene-lined infusion sets and polyvinylchloride tubing are acceptable[1,3,4]

Prior to initiating, and following administration, flush in-line filtered tubing with D5W[1,3]

Additional information

Premedication: ENHERTU is moderately emetogenic, which includes delayed nausea and/or vomiting. Administer prophylactic antiemetic medications per local institutional guidelines for prevention of chemotherapy-induced nausea and vomiting.[1]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis lists fam-trastuzumab deruxtecan-nxki (ENHERTU) as moderate emetic risk and recommends several prophylactic antiemetic regimens to decrease potential nausea/vomiting.[5]

Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation.[1,a]

If a planned dose is delayed or missed, administer as soon as possible; do not wait until the next planned cycle. Administer the infusion at the dose and rate the patient tolerated in the most recent infusion.[1]

Do not re-escalate the ENHERTU dose after a dose reduction is made.[1]

NCCN Guidelines® antiemesis prophylactic and management strategies include[5]:

- Day 1: 5-HT3 receptor antagonist with dexamethasone before fam-trastuzumab deruxtecan-nxki (ENHERTU) infusion
- Days 2 and 3: Dexamethasone or 5-HT3 receptor antagonist

For more information about the prophylaxis and management of acute and delayed emesis prevention, please visit NCCN.org to view the NCCN Guidelines for Antiemesis V.2.2022.

Dose reduction schedule[1]	HER2+ mBC and HER2-low mBC starting dose 5.4 mg/kg
First dose reduction	4.4 mg/kg
Second dose reduction	3.2 mg/kg
Requirement for further dose reduction	Discontinue treatment

[a]See Table 2 in the ENHERTU Prescribing Information for information on dose modifications for adverse reactions.

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Important Safety Information

Indications

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- HER2-positive breast cancer who have received a prior anti-HER2-based regimen either:
  - In the metastatic setting, or
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- HER2-low (IHC 1+ or IHC 2+/ISH-) 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

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

- **Interstitial lung disease (ILD) and pneumonitis, including fatal cases, have been reported with ENHERTU. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue ENHERTU in all patients with Grade 2 or higher ILD/ pneumonitis. Advise patients of the risk and to immediately report symptoms.**
- **Exposure to ENHERTU during pregnancy can cause embryo-fetal harm. Advise patients of these risks and the need for effective contraception.**

Contraindications

None.

Warnings and Precautions

Interstitial Lung Disease / Pneumonitis

Severe, life-threatening, or fatal interstitial lung disease (ILD), including pneumonitis, can occur in patients treated with ENHERTU. A higher incidence of Grade 1 and 2 ILD/pneumonitis has been observed in patients with moderate renal impairment. Advise patients to immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms. Monitor patients for signs and symptoms of ILD. Promptly investigate evidence of ILD. Evaluate patients with suspected ILD by radiographic imaging. Consider consultation with a pulmonologist. For asymptomatic ILD/pneumonitis (Grade 1), interrupt ENHERTU until resolved to Grade 0, then if resolved in ≤28 days from date of onset, maintain dose. If resolved in >28 days from date of onset, reduce dose one level. Consider corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g., ≥0.5 mg/kg/day prednisolone or equivalent). For symptomatic ILD/pneumonitis (Grade 2 or greater), permanently discontinue ENHERTU. Promptly initiate systemic corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g., ≥1 mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks.

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

In patients with metastatic breast cancer and other solid tumors treated with ENHERTU 5.4 mg/kg, ILD occurred in 12% of patients. Fatal outcomes due to ILD and/or pneumonitis occurred in 1.0% of patients treated with ENHERTU. Median time to first onset was 5 months (range: 0.9 to 23).

Neutropenia

Severe neutropenia, including febrile neutropenia, can occur in patients treated with ENHERTU. Monitor complete blood counts prior to initiation of ENHERTU and prior to each dose, and as clinically indicated. For Grade 3 neutropenia (Absolute Neutrophil Count [ANC] <1.0 to 0.5 x 10^9/L) interrupt ENHERTU until resolved to Grade 2 or less, then maintain dose. For Grade 4 neutropenia (ANC <0.5 x 10^9/L), interrupt ENHERTU until resolved to Grade 2 or less, then reduce dose by one level. For febrile neutropenia (ANC <1.0 x 10^9/L and temperature >38.3° C or a sustained temperature of ≥38° C for more than 1 hour), interrupt ENHERTU until resolved, then reduce dose by one level.

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

In patients with metastatic breast cancer and other solid tumors treated with ENHERTU 5.4 mg/kg, a decrease in neutrophil count was reported in 65% of patients. Sixteen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 22 days (range: 2 to 664). Febrile neutropenia was reported in 1.1% of patients.

Left Ventricular Dysfunction

Patients treated with ENHERTU may be at increased risk of developing left ventricular dysfunction. Left ventricular ejection fraction (LVEF) decrease has been observed with anti-HER2 therapies, including ENHERTU. Assess LVEF prior to initiation of ENHERTU and at regular intervals during treatment as clinically indicated. Manage LVEF decrease through treatment interruption. When LVEF is >45% and absolute decrease from baseline is 10-20%, continue treatment with ENHERTU. When LVEF is 40-45% and absolute decrease from baseline is <10%, continue treatment with ENHERTU and repeat LVEF assessment within 3 weeks. When LVEF is 40-45% and absolute decrease from baseline is 10-20%, interrupt ENHERTU and repeat LVEF assessment within 3 weeks. If LVEF has not recovered to within 10% from baseline, permanently discontinue ENHERTU. If LVEF recovers to within 10% from baseline, resume treatment with ENHERTU at the same dose. When LVEF is <40% or absolute decrease from baseline is >20%, interrupt ENHERTU and repeat LVEF assessment within 3 weeks. If LVEF of <40% or absolute decrease from baseline of >20% is confirmed, permanently discontinue ENHERTU. Permanently discontinue ENHERTU in patients with symptomatic congestive heart failure. Treatment with ENHERTU has not been studied in patients with a history of clinically significant cardiac disease or LVEF <50% prior to initiation of treatment.

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ENHERTU®
fam-trastuzumab deruxtecan-nxki
20 mg/mL INJECTION FOR INTRAVENOUS USE

Important Safety Information (cont'd)

Left Ventricular Dysfunction (cont'd)

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

In patients with metastatic breast cancer and other solid tumors treated with ENHERTU 5.4 mg/kg, LVEF decrease was reported in 3.6% of patients, of which 0.4% were Grade 3.

Embryo-Fetal Toxicity

ENHERTU can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risks to a fetus. Verify the pregnancy status of females of reproductive potential prior to the initiation of ENHERTU. Advise females of reproductive potential to use effective contraception during treatment and for 7 months after the last dose of ENHERTU. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for 4 months after the last dose of ENHERTU.

Additional Dose Modifications

Thrombocytopenia

For Grade 3 thrombocytopenia (platelets <50 to 25 x 10^9/L) interrupt ENHERTU until resolved to Grade 1 or less, then maintain dose. For Grade 4 thrombocytopenia (platelets <25 x 10^9/L) interrupt ENHERTU until resolved to Grade 1 or less, then reduce dose by one level.

Adverse Reactions

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

The pooled safety population reflects exposure to ENHERTU 5.4 mg/kg intravenously every 3 weeks in 984 patients in Study DS8201-A-J101 (NCT02564900), DESTINY-Breast01, DESTINY-Breast03, DESTINY-Breast04, and another clinical trial. Among these patients 65% were exposed for >6 months and 39% were exposed for >1 year. In this pooled safety population, the most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (71%), decreased hemoglobin (66%), decreased neutrophil count (65%), decreased lymphocyte count (55%), fatigue (54%), decreased platelet count (47%), increased aspartate aminotransferase (48%), vomiting (44%), increased alanine aminotransferase (42%), alopecia (39%), increased blood alkaline phosphatase (39%), constipation (34%), musculoskeletal pain (32%), decreased appetite (32%), hypokalemia (28%), diarrhea (28%), and respiratory infection (24%).

HER2-Positive Metastatic Breast Cancer

DESTINY-Breast03

The safety of ENHERTU was evaluated in 257 patients with unresectable or metastatic HER2-positive breast cancer who received at least one dose of ENHERTU 5.4 mg/kg intravenously every three weeks in DESTINY-Breast03. The median duration of treatment was 14 months (range: 0.7 to 30).

Serious adverse reactions occurred in 19% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were vomiting, interstitial lung disease, pneumonia, pyrexia, and urinary tract infection. Fatalities due to adverse reactions occurred in 0.8% of patients including COVID-19 and sudden death (one patient each).

ENHERTU was permanently discontinued in 14% of patients, of which ILD/pneumonitis accounted for 8%. Dose interruptions due to adverse reactions occurred in 44% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were neutropenia, leukopenia, anemia, thrombocytopenia, pneumonia, nausea, fatigue, and ILD/pneumonitis. Dose reductions occurred in 21% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were nausea, neutropenia, and fatigue.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (74%), decreased neutrophil count (70%), increased aspartate aminotransferase (67%), decreased hemoglobin (64%), decreased lymphocyte count (55%), increased alanine aminotransferase (53%), decreased platelet count (52%), fatigue (49%), vomiting (49%), increased blood alkaline phosphatase (49%), alopecia (37%), hypokalemia (35%), constipation (34%), musculoskeletal pain (31%), diarrhea (29%), decreased appetite (29%), respiratory infection (22%), headache (22%), abdominal pain (21%), increased blood bilirubin (20%), and stomatitis (20%).

HER2-Low Metastatic Breast Cancer

DESTINY-Breast04

The safety of ENHERTU was evaluated in 371 patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who received ENHERTU 5.4 mg/kg intravenously every 3 weeks in DESTINY-Breast04. The median duration of treatment was 8 months (range: 0.2 to 33) for patients who received ENHERTU.

Serious adverse reactions occurred in 28% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, pneumonia, dyspnea, musculoskeletal pain, sepsis, anemia, febrile neutropenia, hypercalcemia, nausea, pyrexia, and vomiting. Fatalities due to adverse reactions occurred in 4% of patients including ILD/pneumonitis (3 patients); sepsis (2 patients); and ischemic colitis, disseminated intravascular coagulation, dyspnea, febrile neutropenia, general physical health deterioration, pleural effusion, and respiratory failure (1 patient each).

ENHERTU was permanently discontinued in 16% of patients, of which ILD/pneumonitis accounted for 8%. Dose interruptions due to adverse reactions occurred in 39% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were neutropenia, fatigue, anemia, leukopenia, COVID-19, ILD/pneumonitis, increased transaminases, and hyperbilirubinemia.

Important Safety Information (cont'd)

HER2-Low Metastatic Breast Cancer (cont'd)

DESTINY-Breast04 (cont'd)

Dose reductions occurred in 23% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were fatigue, nausea, thrombocytopenia, and neutropenia.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (70%), decreased hemoglobin (64%), decreased neutrophil count (64%), decreased lymphocyte count (55%), fatigue (54%), decreased platelet count (44%), alopecia (40%), vomiting (40%), increased aspartate aminotransferase (38%), increased alanine aminotransferase (36%), constipation (34%), increased blood alkaline phosphatase (34%), decreased appetite (32%), musculoskeletal pain (32%), diarrhea (27%), and hypokalemia (25%).

Use in Specific Populations

- **Pregnancy:** ENHERTU can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risks to a fetus. There are clinical considerations if ENHERTU is used in pregnant women, or if a patient becomes pregnant within 7 months after the last dose of ENHERTU.
- **Lactation:** There are no data regarding the presence of ENHERTU in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with ENHERTU and for 7 months after the last dose.
- **Females and Males of Reproductive Potential:** Pregnancy testing: Verify pregnancy status of females of reproductive potential prior to initiation of ENHERTU. Contraception: *Females*: ENHERTU can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with ENHERTU and for 7 months after the last dose. *Males*: Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for 4 months after the last dose. Infertility: ENHERTU may impair male reproductive function and fertility.
- **Pediatric Use:** Safety and effectiveness of ENHERTU have not been established in pediatric patients.
- **Geriatric Use:** Of the 883 patients with breast cancer treated with ENHERTU 5.4 mg/kg, 22% were ≥65 years and 3.6% were ≥75 years. No overall differences in efficacy within clinical studies were observed between patients ≥65 years of age compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients aged ≥65 years (60%) as compared to younger patients (48%).
- **Renal Impairment:** A higher incidence of Grade 1 and 2 ILD/pneumonitis has been observed in patients with moderate renal impairment. Monitor patients with moderate renal impairment more frequently. The recommended dosage of ENHERTU has not been established for patients with severe renal impairment (CLcr <30 mL/min).
- **Hepatic Impairment:** In patients with moderate hepatic impairment, due to potentially increased exposure, closely monitor for increased toxicities related to the topoisomerase inhibitor. The recommended dosage of ENHERTU has not been established for patients with severe hepatic impairment (total bilirubin >3 times ULN and any AST).

To report SUSPECTED ADVERSE REACTIONS, contact Daiichi Sankyo, Inc. at 1-877-437-7763 or FDA at 1-800-FDA-1088 or fda.gov/medwatch.

Abbreviations: 5-HT3, 5-hydroxytryptamine 3; CBC, complete blood count; CT, computed tomography; D5W, dextrose 5% in water; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; mBC, metastatic breast cancer; NCCN, National Comprehensive Cancer Network.

References: 1. ENHERTU. Prescribing information. Daiichi Sankyo, Inc.; 2022. **2.** OSHA Hazardous Drugs. OSHA. http://www.osha.gov/SLTC/hazardousdrugs/index.html. **3.** Data on file. Daiichi Sankyo, Inc. Basking Ridge, NJ. **4.** Chemical Retrieval on the Web. Polymer database website. https://polymerdatabase.com/polymer%20classes/Polyolefin%20type.html. Accessed January 15, 2021. **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed June 6, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **6.** Kubo K, Azuma A, Kanazawa M, et al; Japanese Respiratory Society Committee. Consensus statement for the diagnosis and treatment of drug-induced lung injuries. *Respir Investig*. 2013;51(4):260-277. **7.** Ripley BA, Kelil T, Gill RR. Deciphering drug-induced interstitial lung disease: a mechanistic approach. *Appl Radiol*. 2016;45(4):9-18. **8.** Cortés J, Kim SB, Chung WP, et al; DESTINY-Breast03 Trial Investigators. Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer. *N Engl J Med*. 2022;386(12):1143-1154.

ILD/PNEUMONITIS SYMPTOM IDENTIFICATION[1,a]

Identification of the signs and symptoms of potentially fatal ILD/pneumonitis is an important aspect of patient management.

Use this guide to help identify symptoms in your patients.

Patients with ILD/pneumonitis may present with symptoms such as[1]:

- Cough
- Trouble breathing or shortness of breath
- Fever
- Other new or worsening breathing symptoms (eg, chest tightness, wheezing)

Advise patients to immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms.

Monitor patients with moderate renal impairment more frequently due to a higher incidence of Grade 1 and 2 ILD/pneumonitis observed in these patients.[1]

[a]Interstitial lung disease includes events that were adjudicated as ILD for ENHERTU: pneumonitis, interstitial lung disease, respiratory failure, organizing pneumonia, acute respiratory failure, lung infiltration, lymphangitis, alveolitis, pneumonia, pulmonary mass, and radiation pneumonitis.

Potential questions to ask your patients to help identify ILD/pneumonitis[6,7]

- ☐ Have you been coughing recently?
- ☐ Is it a dry cough?
- ☐ Have you had any shortness of breath, especially during or after physical activity?
- ☐ Have you experienced any new breathing or respiratory problems?
- ☐ If you already have respiratory problems, have they gotten worse?
- ☐ Have you had a fever?
- ☐ Have you been feeling tired?
- ☐ Have you lost weight?

Promptly investigate evidence of ILD/pneumonitis[8]

- Diagnosis of ILD/pneumonitis requires exclusion of other causes
- Evaluation may include:
  - High-resolution CT
  - Pulmonologist consultation
  - Blood culture and CBC
- All events of ILD/pneumonitis, regardless of severity or seriousness, should be followed until resolution, including after drug discontinuation
- Please see Prescribing Information for monitoring and management guidance

Indications

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  - In the metastatic setting, or
  - In the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy
- HER2-low (IHC 1+ or IHC 2+/ISH-) 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

Selected Information Regarding Warnings and Precautions

ENHERTU is associated with a number of serious, potentially fatal, Warnings and Precautions, including Interstitial Lung Disease/Pneumonitis, Neutropenia, Left Ventricular Dysfunction, Embryo-Fetal Toxicity. Please see Important Safety Information.

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