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

# Expanding the potential of HER2 actionability with HER2-ultralow mBC in eligible patients

## HER2-ultralow status is defined as IHC 0 with membrane staining (any staining of the membrane in >0 and ≤10% of the cancer cells)[1,2]



**~60%**
of HR+/HER2-negative mBC tumors previously considered IHC 0 are **HER2-ultralow**[3,a]



**You may be asked to re-evaluate previous HER2 IHC 0 results to identify all patients who may be eligible for ENHERTU**[1]

**Report all HER2-ultralow results using the 2025 CAP Breast Biomarker Reporting Template**

**Study design:** DESTINY-Breast06 is a Phase 3, international, multicenter, randomized, open-label trial of ENHERTU vs physician's choice of chemotherapy in 866 patients with HR+/HER2-low (IHC 1+ or IHC 2+/ISH–) or HER2-ultralow (IHC 0 with membrane staining) mBC. Patients were eligible if they had disease progression on at least 2 lines of ET in the metastatic setting, or 1 line of ET in the metastatic setting and progressed within 24 months of the start of adjuvant ET or within 6 months of starting 1L ET + CDK4/6 inhibitor in the metastatic setting. Patients in the ENHERTU arm received 5.4 mg/kg IV Q3W and patients in the chemotherapy arm could receive capecitabine, nab-paclitaxel, or paclitaxel. Treatment was continued until unacceptable toxicity or disease progression. The primary endpoint was PFS (BICR) in the HER2-low population (determined by BICR according to RECIST v1.1). Select secondary endpoints included PFS (BICR) in the overall study population (HER2-low and HER2-ultralow); OS in the HER2-low population and in the overall study population; ORR in the HER2-low population and in the overall study population; and DOR in the HER2-low population and in the overall study population.[1,4-6]

[a]As demonstrated in DESTINY-Breast06 screening data. Among the 1856 patients screened for participation in the study, 12% (225 patients) had IHC 0 with absent membrane staining, while 22% (402 patients) were classified as HER2-ultralow, defined as IHC 0 with membrane staining. IHC 1+ was observed in 45% (829 patients), and IHC 2+/ISH- in 21% (385 patients).[3]

## Indication and Important Safety Information

### Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for:

- HER2-Low and HER2-Ultralow Metastatic Breast Cancer
  - As monotherapy for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-authorized test, that has progressed on one or more endocrine therapies in the metastatic setting
  - As monotherapy for the treatment of adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-authorized test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

### Important Safety Information

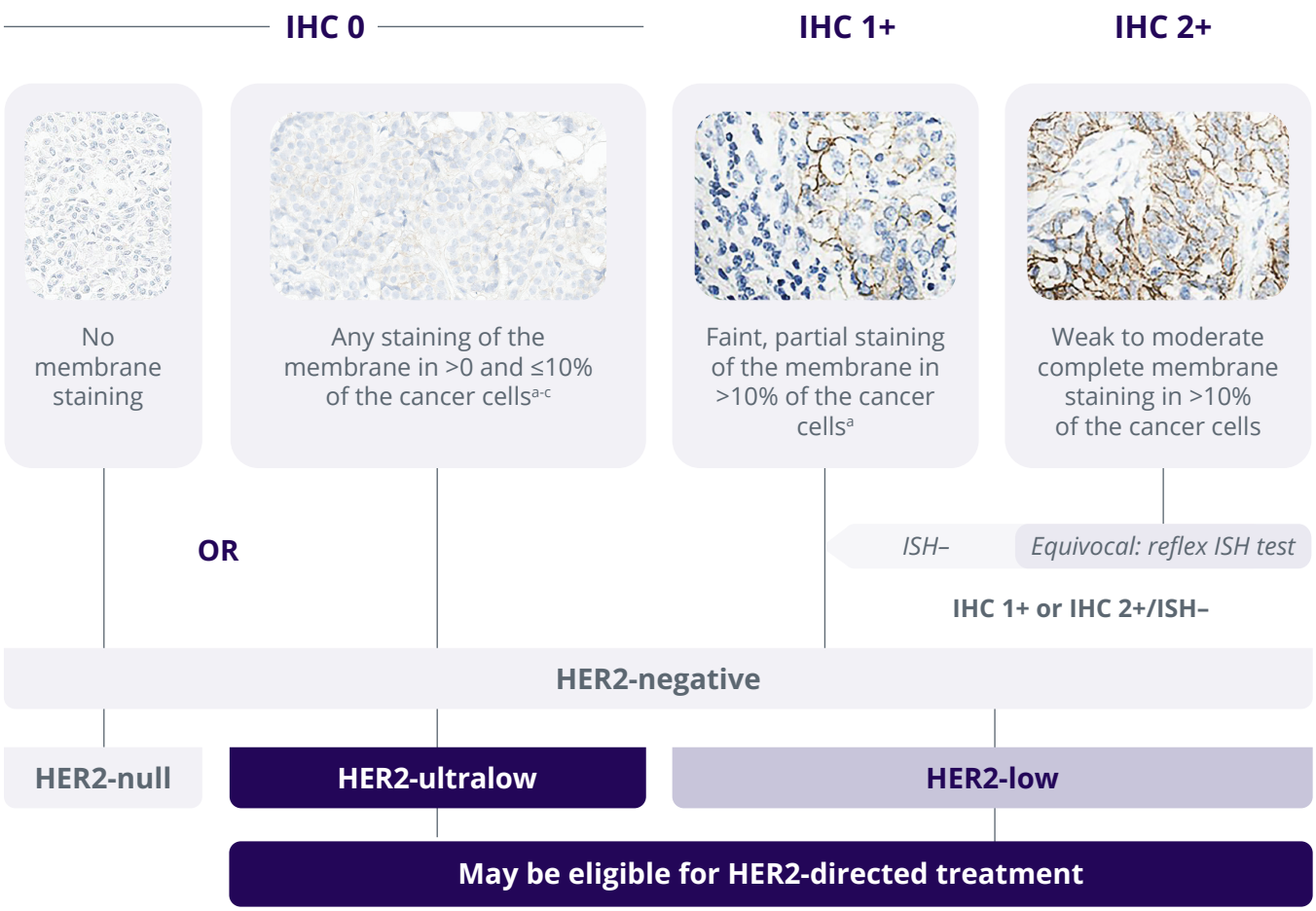
**WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY**

- **Interstitial lung disease (ILD) and pneumonitis, including severe, life-threatening, and 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 on pages 6-9 and throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

# Perform HER2 IHC testing to identify patients with HER2-ultralow mBC who may be eligible for HER2-directed treatment

**Test for HER2-ultralow with IHC using the proposed scoring algorithm based on the PATHWAY HER2 (4B5) FDA-authorized companion diagnostic scoring criteria for breast cancer[1,2,7]**



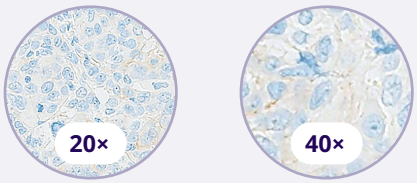

[a]Review at 40x is recommended to discern the presence or absence of any staining such as faint, partial staining.[2]
[b]Recommend re-reading by a second pathologist for cases classified as HER2-null or as HER2-ultralow expression with % of tumor cells ≤5%.[2]
[c]In the HER2-ultralow "IHC 0 with membrane staining" category, partial membranous staining is usually faint but may exhibit stronger intensities, and such rare cases are scored as HER2-ultralow if they do not otherwise qualify for a higher score. Refer to the PATHWAY HER2 (4B5) Interpretation Guide for case examples.[2]

**Please see Important Safety Information on pages 6-9 and throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

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

# Interpret and clearly report HER2-ultralow status

**Use high-power magnification (40x) to discern any staining of the membrane in >0 and ≤10% of the cancer cells[8]**




**According to the updated CAP Breast Biomarker Reporting Template published in June 2025, report HER2-ultralow status by documenting IHC 0+ with membrane staining[9]**

**Recommended reporting for HER2-ultralow[9]**

View 2025 CAP Reporting Template

Specifying "HER2-ultralow" in comments can help the treatment team understand your report

## HER2 by Immunohistochemistry (IHC) Status

- ✓ Negative (Score 0)#
  - ____ No membrane staining detected (0/absent membrane staining)
  - ✓ Membrane staining that is incomplete and is faint/barely perceptible and in ≤10% of tumor cells (0+/with membrane staining)
  - ____ Other (specify): ____

**+Comment(s) on HER2 IHC Results#**

*#Breast cancers with HER2 IHC scores of 0+, 1+, or 2+ (ISH negative) may be eligible for treatment targeting non-amplified levels of HER2 expression in the metastatic setting. Currently, patients with no membrane staining by IHC (0) are ineligible/excluded. Consider using the optional standardized HER2 IHC report comment to explain the clinical relevance of lower levels of HER2 IHC staining in the metastatic setting and definitions of "ultralow and low" HER2 used in clinical trials.*

- ✓ In the DESTINY-Breast04 and 06 trials, "HER2 low" was considered IHC Score 1+ or 2+/ISH negative, and "HER2 ultralow" was HER2 IHC Score of 0 (pattern 0+) with membrane staining that is incomplete and faint/barely perceptible in less than or equal to 10% of tumor cells. Breast cancers with these staining patterns may be eligible for treatment with trastuzumab-deruxtecan in the metastatic setting (but those with no staining, IHC 0, are currently excluded)
- ✓ **Other (specify):** HER2-ultralow

**Utilize the CAP Breast Biomarker Reporting Template to provide consistent communication of potentially actionable results to your multidisciplinary team**

**Please see Important Safety Information on pages 6-9 and throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

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

# Characterization of HER2-ultralow varies across guidelines

## Although scoring criteria and descriptions of HER2 IHC status differ, all are consistent with the HER2-ultralow indication for ENHERTU[1,2,9,10]

| Study/guideline | Scoring criteria | HER2 IHC status description | ENHERTU indication |
|---|---|---|---|
| **DESTINY-Breast06** | Membrane staining that is seen in >0 and ≤10% of tumor cells | IHC 0 with membrane staining | **HER2-ultralow** |
| **PATHWAY HER2 (4B5) Roche/Ventana CDx** | Any staining of the membrane in >0 and ≤10% of the cancer cells | IHC 0 with membrane staining | |
| **2025 CAP Breast Biomarker Reporting Template** | Membrane staining that is incomplete and is faint/barely perceptible and in ≤10% of tumor cells | 0+/with membrane staining | |
| **2023 ASCO-CAP Guidelines** | Membrane staining that is incomplete and is faint/barely perceptible and in ≤10% tumor cells | IHC 0 | |

**Important Safety Information (cont'd)**

**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 1 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.

**Please see Important Safety Information on pages 6-9 and throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

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

# Descriptions of HER2-ultralow status may differ by laboratory

- Terms that indicate HER2-ultralow status may appear in Results, Interpretation, or Comments sections of reports
- Report language and details vary across laboratories, and the term "HER2-ultralow" may not be used in all cases

| Reference laboratory[a] | HER2-ultralow description[b,c] | Location in report |
|---|---|---|
| **Caris Life Sciences**<br>carislifesciences.com<br>888-979-8669 | HER2-Ultralow; Score 0 | Results with Therapy Associations section[d] |
| **Foundation Medicine**<br>foundationmedicine.com<br>888-988-3639 | 0 (HER2-ultralow) | Patient Result table |
| **LabCorp**<br>labcorp.com<br>800-845-6167 | HER2-ultralow | Interpretation section |
| **NeoGenomics Laboratories**<br>neogenomics.com<br>239-768-0600 | 0 with % of cells with incomplete membrane staining that is faint/barely perceptible | Results section |
| **PathGroup**<br>pathgroup.com<br>800-366-5847 | 0 with HER2-ultralow | Results section |
| **Quest Diagnostics**<br>questdiagnostics.com<br>866-697-8378 | 0+ | Results section |
| **Tempus**<br>tempus.com<br>800-739-4137 | 0 with % of cells with incomplete or faint/barely perceptible membrane staining | Results section for score; Comments section for % |

This is not a comprehensive list of all labs that may test for and/or report HER2-low or HER2-ultralow IHC in the US. AstraZeneca and Daiichi Sankyo, Inc. are not affiliated with and do not endorse any of the listed laboratories. This is for information purposes only.

**Your expertise may be needed to help your treating team colleagues identify HER2-ultralow results in laboratory reports**

[a]Testing is available at various labs throughout the United States. The following locations are testing sites that offer relevant HER2 testing. These listings may not be inclusive of all locations. The lab information is provided for informational purposes only. [b]Reflects terminology used by primary laboratory locations; other locations might differ in their reporting. Laboratories typically report the following information in cases of HER2-ultralow mBC: HER2 status (HER2-negative), IHC score (0 or 0+), and staining (incomplete faint membrane staining in ≤10% of tumor cells). [c]HER2-ultralow is defined as a score of IHC 0 with membrane staining that is incomplete and faint/barely perceptible in ≤10% of tumor cells. [d]Ultralow results may also be reported in other sections of the Caris report, including: Important Note (ultralow [IHC 0 with membrane staining]), Immunohistochemistry Results (*ERBB2* [Her2/Neu] Ultralow | Score 0), and Appendix – Protein Expression by Immunohistochemistry (IHC) (*ERBB2* [Her2/Neu]: Negative | Ultralow).

**Please see Important Safety Information on pages 6-9 and throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

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

# Indication and Important Safety Information

## Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for:

- HER2-Low and HER2-Ultralow Metastatic Breast Cancer
  - As monotherapy for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-authorized test, that has progressed on one or more endocrine therapies in the metastatic setting
  - As monotherapy for the treatment of adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-authorized test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

## Important Safety Information

**WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY**

- **Interstitial lung disease (ILD) and pneumonitis, including severe, life-threatening, and 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 1 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 treated with ENHERTU 5.4 mg/kg, ILD occurred in 12% of patients. Median time to first onset was 5.5 months (range: 0.9 to 31.5). Fatal outcomes due to ILD and/or pneumonitis occurred in 0.9% of patients treated with ENHERTU.

#### 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 1 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 1 level.

**Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

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

# Important Safety Information (cont'd)

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)
In patients treated with ENHERTU 5.4 mg/kg, a decrease in neutrophil count was reported in 65% of patients. Nineteen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 22 days (range: 2 to 939). Febrile neutropenia was reported in 1% of patients.

**Left Ventricular Dysfunction**
Patients treated with ENHERTU may be at increased risk of developing left ventricular dysfunction. Left ventricular dysfunction (LVD) has been observed with anti-HER2 therapies, including ENHERTU. Assess left ventricular ejection fraction (LVEF) prior to initiation of ENHERTU and at regular intervals during treatment as clinically indicated. Manage LVD 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.

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)
In patients treated with ENHERTU 5.4 mg/kg, LVD was reported in 4.6% of patients, of which 0.6% were Grade 3 or 4.

**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 1 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 2233 patients in Study DS8201-A-J101 (NCT02564900), DESTINY-Breast01, DESTINY-Breast02, DESTINY-Breast03, DESTINY-Breast04, DESTINY-Breast06, and other clinical trials. Among these patients, 67% 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 decreased white blood cell count (73%), nausea (72%), decreased hemoglobin (67%), decreased neutrophil count (65%), decreased lymphocyte count (60%), fatigue (55%), decreased platelet count (48%), increased aspartate aminotransferase (46%), increased alanine aminotransferase (43%), increased blood alkaline phosphatase (39%), vomiting (38%), alopecia (37%), constipation (32%), decreased blood potassium (32%), decreased appetite (31%), diarrhea (30%), and musculoskeletal pain (24%).

HER2-Low and HER2-Ultralow Metastatic Breast Cancer
*DESTINY-Breast06*
The safety of ENHERTU was evaluated in 434 patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer who received ENHERTU 5.4 mg/kg intravenously once every 3 weeks in DESTINY-Breast06. The median duration of treatment was 11 months (range: 0.4 to 39.6) for patients who received ENHERTU.

**Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

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

# Important Safety Information (cont'd)

**Adverse Reactions (cont'd)**

Serious adverse reactions occurred in 20% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, COVID-19, febrile neutropenia, and hypokalemia. Fatalities due to adverse reactions occurred in 2.8% of patients including ILD (0.7%); sepsis (0.5%); and COVID-19 pneumonia, bacterial meningoencephalitis, neutropenic sepsis, peritonitis, cerebrovascular accident, general physical health deterioration (0.2% each).

ENHERTU was permanently discontinued in 14% of patients. The most frequent adverse reaction (>2%) associated with permanent discontinuation was ILD/pneumonitis. Dose interruptions due to adverse reactions occurred in 48% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were COVID-19, decreased neutrophil count, anemia, pyrexia, pneumonia, decreased white blood cell count, and ILD. Dose reductions occurred in 25% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were nausea, fatigue, decreased platelet count, and decreased neutrophil count.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased white blood cell count (86%), decreased neutrophil count (75%), nausea (70%), decreased hemoglobin (69%), decreased lymphocyte count (66%), fatigue (53%), decreased platelet count (48%), alopecia (48%), increased alanine aminotransferase (44%), increased blood alkaline phosphatase (43%), increased aspartate aminotransferase (41%), decreased blood potassium (35%), diarrhea (34%), vomiting (34%), constipation (32%), decreased appetite (26%), COVID-19 (26%), and musculoskeletal pain (24%).

*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 once 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. 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 decreased blood potassium (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.

**Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

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

# Important Safety Information (cont'd)

- **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 2233 patients treated with ENHERTU 5.4 mg/kg, 28% were ≥65 years and 6% were ≥75 years. No overall differences in efficacy within clinical studies were observed between patients ≥65 years compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients aged ≥65 years (56%) as compared to younger patients (49%).
- **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, monitor for increased adverse reactions related to the topoisomerase inhibitor, DXd. 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.**

**Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

## Abbreviations

1L, first line; ASCO, American Society of Clinical Oncology; BICR, blinded independent central review; CAP, College of American Pathologists; CDK4/6, cyclin-dependent kinases 4 and 6; CDx, companion diagnostic; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor-positive; IHC, immunohistochemistry; ISH, in situ hybridization; IV, intravenous; mBC, metastatic breast cancer; ORR; overall response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

## References

**1.** ENHERTU. Prescribing Information. Daiichi Sankyo, Inc.; 2026. **2.** PATHWAY anti-HER-2/neu (4B5) rabbit monoclonal primary antibody method sheet. 14427US Rev N. 26-01-05. **3.** Viale G, Salgado R, Bardia A, et al. HER2-low and HER2-ultralow status determination in tumors of patients with hormone receptor-positive metastatic breast cancer in DESTINY-Breast06. Presented at: European Society for Medical Oncology; September 13-17, 2024; Barcelona, Spain. **4.** Bardia A, Hu X, Dent R, et al; DESTINY-Breast06 Trial Investigators. Trastuzumab deruxtecan after endocrine therapy in metastatic breast cancer. *N Engl J Med*. 2024;391(22):2110-2122. **5.** Bardia A, Hu X, Dent R, et al; DESTINY-Breast06 Trial Investigators. Supplement to: Trastuzumab deruxtecan after endocrine therapy in metastatic breast cancer. *N Engl J Med*. 2024;391(22):2110-2122. **6.** Bardia A, Hu X, Dent R, et al; DESTINY-Breast06 Trial Investigators. Protocol for: Trastuzumab deruxtecan after endocrine therapy in metastatic breast cancer. *N Engl J Med*. 2024;391(22):2110-2122. **7.** Data on file. Daiichi Sankyo, Inc. Basking Ridge, NJ. **8.** PATHWAY anti-HER-2/neu (4B5) rabbit monoclonal primary antibody interpretation guide for breast cancer. 14991US Rev A. 25-01-28. **9.** College of American Pathologists. Reporting template for reporting results of biomarker testing of specimens from patients with carcinoma of the breast. Accessed March 19, 2025. https://documents.cap.org/documents/New-Cancer-Protocols-March-2025/Breast.Bmk_1.6.0.0.REL.CAPCP.pdf
**10.** Wolff AC, Somerfield MR, Dowsett M, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology-College of American Pathologists guideline update. *Arch Pathol Lab Med*. 2023;147(9):993-1000.

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

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

# Identify HER2-ultralow status for your multidisciplinary colleagues

- Use high-power magnification (40x) to distinguish between IHC 0/absent membrane staining (HER2-null) and IHC 0+/with membrane staining (HER2-ultralow)[8]
- Use consistent terminology when reporting HER2-ultralow results to your multidisciplinary team

**The updated 2025 CAP Breast Biomarker Reporting Template provides structured reporting of HER2-ultralow**

**View template**

**Reporting all HER2-ultralow results may help identify patients who may be eligible for ENHERTU**

**Learn more**

## Indication and Important Safety Information

### Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for:

- HER2-Low and HER2-Ultralow Metastatic Breast Cancer
  - As monotherapy for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-authorized test, that has progressed on one or more endocrine therapies in the metastatic setting
  - As monotherapy for the treatment of adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-authorized test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

### Important Safety Information

**WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY**

- **Interstitial lung disease (ILD) and pneumonitis, including severe, life-threatening, and 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 on pages 6-9 and throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide.**

Daiichi-Sankyo | AstraZeneca

ENHERTU® is a registered trademark of Daiichi Sankyo Company, Limited. © 2026 Daiichi Sankyo, Inc. and AstraZeneca.
PP-US-ENB-4673-2 08/26 US-112466