



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



Patient Access to Treatment

Important Safety Information

Indications

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

- HER2-Positive Early Breast Cancer
 - As neoadjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) Stage II or III breast cancer, as determined by an FDA-authorized test followed by a taxane, trastuzumab, and pertuzumab (THP)
 - As adjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) breast cancer who have residual invasive disease following neoadjuvant trastuzumab (with or without pertuzumab) and taxane-based treatment
- HER2-Positive Metastatic Breast Cancer
 - In combination with pertuzumab as first-line treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH+) breast cancer, as determined by an FDA-authorized test
 - As monotherapy for the treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH+) 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 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
- HER2-Mutant Unresectable or Metastatic Non-Small Cell Lung Cancer (NSCLC)
 - As monotherapy for the treatment of adult patients with unresectable or metastatic NSCLC whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-authorized test, and who have received a prior systemic therapy

This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- HER2-Positive Locally Advanced or Metastatic Gastric Cancer
 - As monotherapy for the treatment of adult patients with locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen
- HER2-Positive (IHC 3+) Unresectable or Metastatic Solid Tumors
 - As monotherapy for the treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options

This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Please see additional Important Safety Information throughout, and see full Prescribing Information, including **Boxed WARNINGS, and **Medication Guide**.**

ENHERTU4U represents a suite of support programs to help patients afford and access ENHERTU

ENHERTU4U offers support for eligible patients who have been prescribed ENHERTU



Access

Support options are available to help your patients access ENHERTU. Enroll today for help with benefit verifications and understanding prior authorizations. See pages 3-4 for more information.



Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement. See pages 7-23.



Affordability

Multiple options are available to help eligible patients afford their treatment. See pages 5-6 for programs and enrollment information.



Distribution

ENHERTU is available through a network of select specialty distributors and specialty pharmacies. See pages 24-25 to learn more about how you can order ENHERTU.

ENHERTU4U does not guarantee access or cost savings.

Support from ENHERTU4U is available over the phone and on the web



1-833-ENHERTU
(1-833-364-3788)



www.ENHERTU4U.com

Important Safety Information (cont'd)

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.

Please see additional Important Safety Information throughout, and see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

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Access

Support to help patients access ENHERTU

ENHERTU4U provides comprehensive access support for patients who have been prescribed ENHERTU. Our specialists can help with benefit verification, prior authorization (PA) assistance, and pharmacy research and coordination.

To request support for your patient, please complete and sign pages 1 and 3 of the patient enrollment form and fax it to 1-866-760-5917. A signature is required from both prescriber *and* patient. You may also call **1-833-ENHERTU (1-833-364-3788)** to enroll your patient over the phone.

Upon receiving a completed enrollment form, our team will complete the benefit verification within 1 business day and provide your office with the PA requirements and required forms to help obtain insurance approval for your patient's treatment.

Once you submit the PA request, ENHERTU4U will follow up with your patient's insurance company to help ensure that you receive a coverage decision.

Patients will be assessed for a temporary free supply if they experience a coverage delay of greater than 5 business days. Please call **1-833-ENHERTU (1-833-364-3788)** to learn more.

ENHERTU4U Enrollment Form

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Support Requested (check only those that apply)

☐ Benefits Investigation (Please choose your preferred acquisition method below. Based on the preference, ENHERTU4U will research the pharmacy and/or medical benefits for your patient.)

☐ Buy & Bill

☐ Specialty Pharmacy Provider (SPP). Preferred SPP: _____

☐ Unknown

☐ Co-Pay Support (Note: You may also visit www.patientsavingsku.com for direct enrollment into the ENHERTU Patient Co-pay Savings Program (eligibility rules apply))

☐ Prior Authorization Support

☐ Claims/Billing/Reimbursement Support (Please attach a copy of the claim submitted and Explanation of Benefits)

☐ Appeals Support (Please attach a copy of the denial letter)

Please complete form, sign, and fax to **1-866-760-5917**. For questions or assistance, please call ENHERTU4U, Monday through Friday, 9 AM - 6 PM ET, at **1-833-ENHERTU (1-833-364-3788)**.

To enroll in the ENHERTU Patient Assistance Program, visit www.ENHERTU4U.com/hcp/affordability. (Eligibility rules apply)

1 Patient Information

First Name: _____ Last Name: _____ Patient DOB: ____/____/____ Gender: ☐ M ☐ F

Address: _____ City: _____ State: _____ ZIP: _____

Preferred Phone #: ☐ Home ☐ Mobile _____ Patient Email: _____

Alternate Contact Name: _____ Relationship to Patient: _____

Alternate Contact Phone #: _____ Patient preferred language (if other than English): _____

Okay to contact patient? ☐ Yes ☐ No Okay to leave a detailed voicemail? ☐ Yes ☐ No

Patient Authorization

(I have read and agree to the Patient Authorization included on page 2)

Patient Signature/Legal Representative MM DD YYYY _____

Printed Name/Relationship to Patient (if applicable) _____

Support Programs (Savings Program and Additional Services)

(I have read and agree to the Support Programs Authorization included on page 2)

Patient Signature/Legal Representative MM DD YYYY _____

Printed Name/Relationship to Patient (if applicable) _____

2 Insurance Information Please include front and back copies of all medical and pharmacy cards or complete this section.

☐ Commercial/Private Insurance ☐ Medicare/Medicaid/Ticare ☐ No Insurance

	Primary Medical Insurance	Secondary Medical Insurance	Pharmacy Insurance
Insurance Provider			
Insurance Phone #			
Cardholder Name (if not the patient)			
Cardholder DOB			
Policy #			
Group #			
BI/PCN	X	X	

3 Provider Information

Prescriber Name: _____ Specialty: _____

Practice Name: _____ Office Contact Name: _____

Address: _____ City: _____ State: _____ ZIP: _____

Phone #: _____ Fax #: _____ Email: _____

Prescriber NPI #: _____ Site Tax ID #: _____

PTAN: _____ Other Provider ID (if applicable): _____

Alternate Office Contact Name: _____ Alternate Office Contact Phone #: _____ Alternate Office Contact Email: _____

Please see Important Safety Information on pages 4-7, and see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.



1-833-ENHERTU (1-833-364-3788)
8 AM - 6 PM ET, Monday through Friday



www.ENHERTU4U.com



1-866-760-5917

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Interstitial Lung Disease / Pneumonitis (cont'd)

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. In the adjuvant HER2+ breast cancer setting, if drug-induced ILD is suspected, rule out radiotherapy-related pneumonitis. If only radiotherapy-related pneumonitis is suspected, consider interruption of ENHERTU for Grade 2 and permanently discontinue ENHERTU for Grade ≥ 3 .

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+)
(5.4 mg/kg)

ENHERTU as Monotherapy

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.

ENHERTU in Combination with Pertuzumab

In patients treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), ILD occurred in 12% of patients. Median time to first onset was 8.0 months

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4U

Access

Affordability

Coding & Reimbursement

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Important Safety Information



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PA considerations

PA requirements vary by health plan. Please be prepared to include the following information when you submit the PA request. ENHERTU4U will provide you with a list of the PA requirements and appropriate forms after we complete the benefit investigation.

1. Most PA forms will require the following information:

- ☐ Patient information, including insurance policy number and date of birth
- ☐ Physician and facility information, including name, NPI number, and tax ID number
- ☐ Date of service
- ☐ Relevant procedure codes for services/products to be performed/provided
- ☐ Setting of care

2. Some PA forms may require a letter of medical necessity. Please visit www.ENHERTU4U.com for a sample. Be sure to include the provider ID number on the letter.

3. PA approval for ENHERTU may require specific information, such as:

- ☐ ENHERTU indication statement
- ☐ ENHERTU Prescribing Information
- ☐ Documentation that the patient's tumor has spread
- ☐ Documentation of related biomarker testing
- ☐ Previous therapy(ies), including length of therapy and reason for discontinuation

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

(range: 0.6 to 33.8). Fatal outcomes due to ILD and/or pneumonitis occurred in 0.5% of patients treated with ENHERTU in combination with pertuzumab.

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, ILD occurred in 4.4% of patients. Median time to first onset was 2.7 months (range: 1.1 to 6.0). Fatal outcomes due to ILD and/or pneumonitis occurred in 1 patient (0.3%) treated with ENHERTU followed by THP.

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, ILD occurred in 10% of patients. Median time to first onset was 2.8 months (range: 1.2 to 21).

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 $0.5 \times 10^9/L$), interrupt ENHERTU until resolved to Grade 2 or less, then maintain dose. For Grade 4 neutropenia (ANC $<0.5 \times 10^9/L$), interrupt ENHERTU until resolved to Grade 2 or less, then reduce dose by 1 level. For febrile neutropenia (ANC $<1.0 \times 10^9/L$ and temperature $>38.3^\circ C$ or a sustained temperature of $\geq 38^\circ C$ for more than 1 hour), interrupt ENHERTU until resolved, then reduce dose by 1 level.

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+) (5.4 mg/kg)

ENHERTU as Monotherapy

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.

ENHERTU in Combination with Pertuzumab

In patients treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), decreased neutrophil count occurred in 79% of patients. Median time to first onset was 22 days (range: 5 to 994). Twenty-nine percent had Grade 3 or 4 decreased neutrophil count. Febrile neutropenia was reported in 2.6% of patients.

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Affordability

Options are available to help your patients who are prescribed ENHERTU afford their treatment

ENHERTU Patient Savings Program

The goal of the ENHERTU Patient Savings Program is to remove cost as a barrier for eligible commercially insured patients by assisting with their out-of-pocket costs for ENHERTU.

**PAY AS
LITTLE AS**
\$0

Eligible patients with a valid prescription for ENHERTU may pay as little as \$0 per infusion and \$0 out-of-pocket costs for ENHERTU. The annual benefit can be used for the cost of the drug itself, and may also cover up to \$100 in infusion costs per administration.* There are no income requirements to participate in the program.

*Patients who are residents of Massachusetts or Rhode Island are not eligible for infusion administration assistance.



Program eligibility

- Must be a resident of the United States or Puerto Rico
- Patients must have commercial health insurance that covers medication costs for ENHERTU, but not the full cost to the patient
- Patients are ineligible if prescriptions are paid by any state or other federally funded programs, including, but not limited to, Medicare Part B, Medicare Part D, Medicaid, Medigap, VA, or TRICARE, or where prohibited by law. Eligibility rules apply. Additional restrictions may apply
- Offer is invalid for all claims or transactions submitted more than 180 days from the date on the Explanation of Benefits (EOB)

Full Eligibility Criteria and Terms and Conditions can be found at www.ENHERTU4U.com.



How to enroll

Patient enrollment may be done quickly and easily at www.patientsavings4u.com.

1. If you think your patient meets the eligibility requirements, you may enroll them in the ENHERTU Patient Savings Program at www.patientsavings4u.com.
2. Submit all appropriate patient information.
3. If your patient is approved, you may utilize the Patient Savings Program to cover a patient's remaining balance.

If you need assistance enrolling a patient or have questions, please contact ENHERTU4U at **1-833-ENHERTU (1-833-364-3788)**.



Submitting ENHERTU claims from buy-and-bill physician's offices

1. Submit ENHERTU claim to patient's primary insurance plan following administration.
2. After receiving EOB, review to determine exact amount your patient owes for ENHERTU.
3. Submit a claim on behalf of the patient at www.patientsavings4u.com or by calling ENHERTU4U at **1-833-ENHERTU (1-833-364-3788)** for the remaining ENHERTU out-of-pocket costs.
4. After the ENHERTU Patient Savings Program has reviewed the claim, you will be notified if the claim is approved. If approved, the patient's virtual debit card will be loaded with the approved amount. Process a debit card transaction to remove funds from the card.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, a decrease in neutrophil count was reported in 58% of patients. Seventeen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 42 days (range: 11 to 165). Febrile neutropenia was reported in 0.9% of patients.

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, a decrease in neutrophil count was reported in 72% of patients. Fifty-one percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 16 days (range: 4 to 187). Febrile neutropenia was reported in 4.8% of patients.

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Affordability

Options are available to help your patients who are prescribed ENHERTU afford their treatment

Patient Assistance Programs

These programs are designed to help qualifying uninsured, underinsured, or Medicare patients who are having financial difficulty affording their medication. Call **1-833-ENHERTU (1-833-364-3788)** 8 AM – 6 PM ET, Monday through Friday to learn more.

The Patient Assistance Programs (PAP) provide ENHERTU to qualifying patients at no cost. Eligibility rules apply.

To enroll your patients, please visit www.ENHERTU4U.com/hcp/affordability, complete the PAP enrollment form, and fax it to 1-833-904-1851.

Please visit www.ENHERTU4U.com to see full eligibility requirements.

General referral to independent charitable patient assistance foundations

Assistance may be available through independent foundations. Visit www.ENHERTU4U.com/hcp/affordability or call ENHERTU4U to learn more at **1-833-ENHERTU (1-833-364-3788)**. ENHERTU4U does not guarantee support by independent foundations. Each foundation sets their own eligibility requirements and support determinations.



Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

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.

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+)
(5.4 mg/kg)

ENHERTU as Monotherapy

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.

ENHERTU in Combination with Pertuzumab

In patients treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), LVEF decrease was reported in 11% of patients, of which 2.1% were Grade 3 or 4.

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, LVD was reported in 1.3% of patients, of which 0.3% were Grade 3.

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, no clinical adverse events of heart failure were reported; however, on echocardiography, 8% were found to have asymptomatic Grade 2 decrease in LVEF.

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Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement



ENHERTU4U provides support to answer your reimbursement questions

Utilizing appropriate codes on claim forms is required in order to obtain timely and appropriate reimbursement for ENHERTU.

The suggestions contained in this resource are for example only. Daiichi Sankyo/AstraZeneca make no representation that the information is accurate or that it will comply with the requirements of any particular payer/insurer. Providers are solely responsible for determining the billing and coding requirements applicable to any payer/insurer. The information provided here is not intended to be conclusive or exhaustive, and is not intended to replace the guidance of a qualified professional advisor. No warranties or guarantees, expressed or implied, are made concerning the accuracy or appropriateness of this information for your particular use. The use of this information does not guarantee payment or that any payment received will cover your costs.



ENHERTU4U can help with the appeals process

In some cases, payers may deny your initial claim for ENHERTU. When this happens, we are here to help. Please fax a completed Patient Enrollment Form and the explanation of benefits with reason for denial to 1-866-760-5917 for assistance.

Upon request, we will provide you with payer-specific appeals requirements. You will need to provide a formal letter appealing the denial to the payer. A peer-to-peer review may also be required by the health plan. You can find an example appeal letter, peer-to-peer review resource, and more at www.ENHERTU4U.com.

The information provided here is not intended to be conclusive or exhaustive, and is not intended to replace the guidance of a qualified professional advisor. No warranties or guarantees, expressed or implied, are made concerning the accuracy or appropriateness of this information for your particular use. The use of this information does not guarantee payment or that any payment received will cover your costs.



1-833-ENHERTU (1-833-364-3788)
8 AM – 6 PM ET, Monday through Friday



www.ENHERTU4U.com



1-866-760-5917

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

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

Adverse Reactions

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+)
(5.4 mg/kg)

ENHERTU as Monotherapy

The pooled safety population reflects exposure to ENHERTU 5.4 mg/kg intravenously every 3 weeks in 2233 patients in Study

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Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement

National Drug Code (NDC)

10-digit NDC

Code	Description
65597-406-01	One 100 mg single-dose vial

11-digit NDC

Code	Description
65597-0406-01	One 100 mg single-dose vial

Healthcare Common Procedure Coding System (HCPCS) Code¹

Code	Description	Vial Size	Billing Units
J9358	Injection, fam-trastuzumab deruxtecan-nxki, 1 mg	100 mg	100

Current Procedural Terminology (CPT)[®] Code¹

Code	Description
96365	Intravenous infusion, up to 1 hour.
96366	Each additional hour of infusion.
96372	Therapeutic, prophylactic, or diagnostic injection (subcutaneous or intramuscular).
96401	Chemotherapy administration, subcutaneous or intramuscular, non-hormonal anti-neoplastic.
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug

General Evaluation and Management (E/M) Codes¹

Code	Description
99211	Minimal visit (usually for a quick follow-up with low complexity).
99212	Problem-focused visit (low complexity, brief visit), 10 minutes must be met or exceeded.
99213	Expanded problem-focused visit (moderate complexity), 10 minutes must be met or exceeded.
99214	Detailed visit (moderate-to-high complexity, longer time), 30 minutes must be met or exceeded.
99215	Comprehensive visit (high complexity, lengthy reassessment), 40 minutes must be met or exceeded.
99202	Straightforward complexity, 15 minutes must be met or exceeded.
99203	Moderate complexity, 30 minutes must be met or exceeded.
99204	High complexity, 45 minutes must be met or exceeded.
99205	Very high complexity, typically for complicated cases, 60 minutes must be met or exceeded.

Medicare-Specific Evaluation and Management (E/M) Codes¹

Code	Description
G0379	Direct admission of a patient for observation services.
G0463	Hospital outpatient clinic visit for the assessment and management of a patient.

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Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement

Telehealth Evaluation and Management (E/M) Codes²

Please note: only CPT code 98016 is appropriate for Medicare use. Claims for Medicare beneficiaries may also use existing E/M codes with appropriate modifiers and place of service codes when the geographic location and site of service restrictions are met. See below

Code	Description
98000 - 98003	<i>Synchronous audio-video visit for the evaluation and management of a new patient which requires a medically appropriate history and/or examination and...</i>
98000	straightforward medical decision-making. 15 minutes must be met or exceeded
98001	low medical decision-making. When using total time on the date of the encounter for code selection, 30 minutes must be met or exceeded
98002	moderate medical decision-making. When using total time on the date of the encounter for code selection, 45 minutes must be met or exceeded
98003	high medical decision-making. When using total time on the date of the encounter for code selection, 60 minutes must be met or exceeded

Code	Description
98004 - 98007	<i>Synchronous audio-video visit for the evaluation and management of an established patient which requires a medically appropriate history and/or examination and...</i>
98004	straightforward medical decision-making. 10 minutes must be met or exceeded
98005	low medical decision-making. When using total time on the date of the encounter for code selection, 20 minutes must be met or exceeded
98006	moderate medical decision-making. When using total time on the date of the encounter for code selection, 30 minutes must be met or exceeded
98007	high medical decision-making. When using total time on the date of the encounter for code selection, 40 minutes must be met or exceeded

Code	Description
98008 - 98011	<i>Synchronous audio-only visit for the evaluation and management of a new patient, which requires a medically appropriate history and/or examination,</i>
98008	straightforward medical decision-making and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 15 minutes must be met or exceeded
98009	low medical decision making, and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 30 minutes must be met or exceeded.
98010	moderate medical decision making, and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 45 minutes must be met or exceeded.
98011	high medical decision making, and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 60 minutes must be met or exceeded. (For services 75 minutes or longer, use prolonged services code 99417)

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Telehealth Evaluation and Management (E/M) Codes² (cont'd)

Code	Description
98012 - 98016	Synchronous audio-only visit for the evaluation and management of an established patient, which requires a medically appropriate history and/or examination,
98012	straightforward medical decision-making and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 10 minutes must be met or exceeded
98013	low medical decision making, and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 20 minutes must be met or exceeded.
98014	moderate medical decision making, and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 30 minutes must be met or exceeded.
98015	high medical decision making, and more than 10 minutes of medical discussion. When using total time on the date of the encounter for code selection, 40 minutes must be met or exceeded. (For services 55 minutes or longer, use prolonged services code 99417.)

Code	Description
98016	brief communication technology-based service (eg, virtual check-in) by a physician or other qualified health care professional who can report evaluation and management services, provided to an established patient, not originating from a related evaluation and management service provided within the previous 7 days nor leading to an evaluation and management service or procedure within the next 24 hours or soonest available appointment, (5-10 minutes of medical discussion)

Modifier Codes³

Code	Description
Modifier 25	Used when an E/M service is performed on the same day as another procedure.
Modifier 91	Used to indicate a laboratory test repeated on the same day for the same patient.
Modifier 93	Medicare telehealth service was furnished using audio-only communication technology.
Modifier FQ	Medicare telehealth service was furnished using audio-only communication technology; specific to Federally Qualified Health Centers or Rural Health Clinics

Place of Service Codes⁴

Code	Location	Description
02	Telehealth provided other than in patient's home	Patient is not located in their home when receiving health services or health related services through telecommunication technology
10	Telehealth provided in patient's home	Patient is located in their home (which is a location other than a hospital or other facility where the patient receives care in a private residence) when receiving health services or health related services through telecommunication technology.

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

DS8201-A-J101 (NCT02564900), DESTINY-Breast01, DESTINY-Breast02, DESTINY-Breast03, DESTINY-Breast04, DESTINY-Breast06, DESTINY-Lung01, DESTINY-Lung02, DESTINY-CRC02, and DESTINY-PanTumor02. 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

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Place of Service Codes⁴ (cont'd)

11	Office	Location, other than a hospital, skilled nursing facility, military treatment facility, community health center, state or local public health clinic, or intermediate care facility, where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.
19	Off Campus Outpatient Hospital	A portion of an off-campus hospital provider based department which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.
22	On Campus Outpatient Hospital	A portion of a hospital's main campus which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.

Revenue Code⁵

Code	Description
0636	Drugs requiring detailed coding (Pharmacy extension series 063X)

ICD-10-CM Codes

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Examples of primary cancer of anal canal, anus ICD-10-CM codes⁶

Cancer of anal canal, anus sites

ICD-10-CM	Description
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

blood alkaline phosphatase (39%), vomiting (38%), alopecia (37%), constipation (32%), decreased blood potassium (32%), decreased appetite (31%), diarrhea (30%), and musculoskeletal pain (24%).

ENHERTU in Combination with Pertuzumab

The pooled safety population reflects exposure to ENHERTU 5.4 mg/kg in combination with pertuzumab intravenously every 3 weeks in 431 patients in DESTINY-Breast07 (n=50), and DESTINY-Breast09 (n=381). Among these patients, 86% were exposed for >6 months and 73% 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 (86%), decreased hemoglobin (80%), decreased neutrophil count (79%), nausea (74%), increased alanine aminotransferase (65%), diarrhea (64%), increased aspartate aminotransferase (63%), decreased lymphocyte count (61%), decreased platelet count (55%), increased blood alkaline phosphatase (54%), decreased blood potassium (54%), fatigue (53%), alopecia (48%), vomiting (46%), upper respiratory tract infection (32%), constipation (31%), decreased appetite (31%), decreased weight (28%), musculoskeletal pain (23%), increased blood bilirubin (23%), and abdominal pain (22%).

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Examples of primary biliary cancer ICD-10-CM codes⁶

Biliary cancer sites

ICD-10-CM	Description
C22.1	Intrahepatic bile duct carcinoma
C23.0	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified

Examples of primary bladder cancer ICD-10-CM codes⁶

Bladder cancer sites

ICD-10-CM	Description
C65.1	Malignant neoplasm of the right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C66.1	Malignant neoplasm of the right ureter
C66.2	Malignant neoplasm of the left ureter
C66.9	Malignant neoplasm of unspecified ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C68.0	Malignant neoplasm of urethra
C68.1	Malignant neoplasm of paraurethral glands
C68.8	Malignant neoplasm of overlapping sites of urinary organs
C68.9	Malignant neoplasm of urinary organ, unspecified
D09.0	Carcinoma in situ of bladder

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

HER2-Positive Early Breast Cancer

DESTINY-Breast11

The safety of ENHERTU followed by THP was evaluated in 320 patients with HER2-positive (IHC 3+ or ISH+) early breast cancer who received at least 1 dose of ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11. ENHERTU was administered by intravenous infusion once every three weeks for 4 cycles followed by THP for 4 cycles. The median duration of treatment was 5.6 months (range: 0.7 to 9.1) for patients who received ENHERTU followed by THP.

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Examples of primary bladder cancer ICD-10-CM codes⁶ (cont'd)

Personal history

ICD-10-CM	Description
Z85.51	Personal history of malignant neoplasm of bladder
Z85.59	Personal history of malignant neoplasm of other urinary tract organ

Examples of primary breast cancer ICD-10-CM codes⁶

Primary breast cancer sites

ICD-10-CM	Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

Serious adverse reactions occurred in 11% of patients receiving ENHERTU followed by THP, including COVID-19 (0.9%) and ILD/pneumonitis (0.6%). Fatal adverse reactions occurred in 0.6% of patients, including ILD/pneumonitis and death not otherwise specified (1 patient each).

In patients treated with ENHERTU followed by THP, the permanent discontinuation of ENHERTU due to adverse reactions occurred in 1.3%, of which ILD/pneumonitis accounted for 0.6%. Dose interruptions of ENHERTU due to adverse reactions occurred in 11% of patients. The most frequent adverse reactions (>2%) associated with dose interruption

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Examples of primary breast cancer ICD-10-CM codes⁶ (cont'd)

Primary breast cancer sites (cont'd)

ICD-10-CM	Description
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

were decreased neutrophil count and COVID-19. Dose reductions of ENHERTU occurred in 2.5% of patients treated with ENHERTU.

The most common ($\geq 20\%$) adverse reactions in patients treated with ENHERTU followed by THP, including laboratory abnormalities, were decreased hemoglobin (83%), increased alanine aminotransferase (79%), increased aspartate aminotransferase (74%), decreased white blood cell count (67%), nausea (65%), peripheral neuropathy (59%), diarrhea (59%), decreased neutrophil count (58%), alopecia (48%), fatigue (41%), decreased lymphocyte count (40%), rash (31%), musculoskeletal pain (30%), decreased blood potassium (29%), constipation (29%), vomiting (29%), stomatitis (23%), and decreased appetite (20%).

DESTINY-Breast05

The safety of ENHERTU was evaluated in 806 patients with HER2-positive breast cancer with residual invasive disease following neoadjuvant HER2-targeted therapy who then received at least one dose of ENHERTU 5.4 mg/kg. ENHERTU was administered by intravenous infusion once every three weeks for 14 cycles. The median duration of treatment was 10 months (range: 0.7 to 16) for patients who received ENHERTU.

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Examples of primary breast cancer ICD-10-CM codes⁶ (cont'd)

Primary breast cancer sites (cont'd)

ICD-10-CM	Description
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C50.A0	Malignant inflammatory neoplasm of unspecified breast
C50.A1	Malignant inflammatory neoplasm of right breast
C50.A2	Malignant inflammatory neoplasm of left breast

Genetic susceptibility

ICD-10-CM	Description
Z15.01	Genetic susceptibility to malignant neoplasm of breast

Personal history

ICD-10-CM	Description
Z85.3	Personal history of malignant neoplasm of breast

Examples of primary cervical cancer ICD-10-CM codes⁶

Cervical cancer sites

ICD-10-CM	Description
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

Serious adverse reactions occurred in 17% of patients receiving ENHERTU. Serious adverse reactions in $\geq 1\%$ of patients who received ENHERTU were ILD/pneumonitis, radiation pneumonitis, pneumonia, and platelet count decreased. Fatal adverse reactions occurred in 0.4% of patients including ILD/pneumonitis (2 patients) and respiratory tract infection (1 patient).

Permanent discontinuation of ENHERTU due to an adverse reaction occurred in 18% of patients. The adverse reaction which resulted in permanent discontinuation of ENHERTU $>2\%$ included ILD/pneumonitis. Dose interruptions of ENHERTU due to an adverse reaction occurred in 50% of patients. Adverse reactions which required dosage interruptions in $>2\%$ included radiation pneumonitis, neutrophil count decreased, COVID-19, white blood cell count decreased, ILD/pneumonitis, platelet count decreased, upper respiratory tract infection, fatigue, cough, and pyrexia. Dose reductions of ENHERTU due to an adverse reaction occurred in 26% of patients. Adverse reactions which required dose reductions in $>2\%$ of patients included nausea, fatigue, platelet count decreased, ILD/pneumonitis, and neutrophil count decreased.

The most common ($\geq 20\%$) adverse reactions, including laboratory abnormalities, in patients receiving ENHERTU were decreased white blood cell count (80%), decreased lymphocyte count (72%), decreased neutrophil count (72%), nausea (71%), decreased hemoglobin (61%), increased aspartate aminotransferase (60%), fatigue (54%), increased alanine aminotransferase (53%), decreased platelet count (46%), increased blood alkaline phosphatase (39%), constipation (32%), vomiting (31%), decreased blood potassium (27%), diarrhea (23%), musculoskeletal pain (23%), and decreased appetite (20%).

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Examples of primary colorectal cancer ICD-10-CM codes⁶

Colorectal cancer sites

ICD-10-CM	Description
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum

Personal history

ICD-10-CM	Description
Z85.038	Personal history of other malignant neoplasm of large intestine

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

ILD was reported in 17% of patients receiving ENHERTU, which included COVID-19 pneumonia, interstitial lung disease, lung opacity, organizing pneumonia, pneumocystis jirovecii pneumonia, pneumonia, and pneumonitis which was adjudicated as ILD (irrespective of causality). Adjudicated drug-related ILD for ENHERTU was 10% for all Grades and 0.9% for Grades 3 or 4.

HER2-Positive Metastatic Breast Cancer

DESTINY-Breast09

The safety of ENHERTU 5.4 mg/kg in combination with pertuzumab was evaluated in DESTINY-Breast09, a randomized, three-arm, multicenter study including 763 patients with HER2-positive (IHC 3+ or ISH+) unresectable or metastatic breast cancer. Three hundred eighty-one patients received ENHERTU in combination with pertuzumab and 382 patients received THP (taxane [docetaxel or paclitaxel], trastuzumab, and pertuzumab). Among patients who received ENHERTU in combination with pertuzumab, the median duration of treatment was 22 months (range: 0.3 months to 44.5 months).

Serious adverse reactions occurred in 27% of patients receiving ENHERTU in combination with pertuzumab. Serious adverse reactions in >1% of patients were diarrhea, pneumonia, febrile neutropenia, hypokalemia, vomiting, ILD, pulmonary embolism, and sepsis. Fatalities due to adverse reactions occurred in 3.4% of patients including pneumonia (n=3), ILD (n=2), sepsis (n=2), pulmonary embolism, septic shock, acute kidney injury, dyspnea, febrile neutropenia, and intestinal ischemia (1 patient each).

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Examples of primary endometrial cancer ICD-10-CM codes⁶

Endometrial cancer sites

ICD-10-CM	Description
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified

Personal history

ICD-10-CM	Description
Z85.42	Personal history of malignant neoplasm of other parts of uterus

Examples of primary esophageal cancer ICD-10-CM codes⁶

Esophageal cancer sites

ICD-10-CM	Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

ENHERTU was discontinued for adverse reactions in 21% of patients. The most frequent adverse reaction (>2%) associated with permanent discontinuation was ILD/pneumonitis (6%). Dose interruptions due to adverse reactions occurred in 69% of patients. The most frequent adverse reactions (>2%) associated with dose interruption were COVID-19, neutropenia, upper respiratory tract infection, fatigue, anemia, hypokalemia, ILD/pneumonitis, thrombocytopenia, pneumonia, diarrhea, transaminase increased, leukopenia, cough, pyrexia, decreased appetite, and blood bilirubin increased. Dose reductions occurred in 46% of patients treated with ENHERTU in combination with pertuzumab. The most frequent adverse reactions (>2%) associated with dose reduction were fatigue, neutropenia, nausea, diarrhea, ILD/pneumonitis, thrombocytopenia, vomiting, transaminases increased, decreased weight, febrile neutropenia, and hypokalemia.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased white blood cell count (87%), decreased hemoglobin (80%), decreased neutrophil count (78%), nausea (75%), increased alanine aminotransferase (66%), diarrhea (64%), increased aspartate aminotransferase (62%), decreased lymphocyte count (62%), decreased platelet count (56%), increased blood alkaline phosphatase (55%), decreased blood potassium (54%), fatigue (53%), alopecia (48%), vomiting (46%), upper respiratory tract infection (33%), constipation (33%), decreased appetite (32%), decreased weight (30%), COVID-19 (28%), musculoskeletal pain (24%), increased blood bilirubin (23%), and abdominal pain (23%).

DESTINY-Breast03

The safety of ENHERTU was evaluated in 257 patients with unresectable or metastatic HER2-positive breast cancer who received at least 1 dose of ENHERTU 5.4 mg/kg intravenously once every 3 weeks in DESTINY-Breast03. The median duration of treatment was 14 months (range: 0.7 to 30) for patients who received ENHERTU.

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Examples of primary gastric cancer ICD-10-CM codes⁶

Primary gastric cancer sites

ICD-10-CM	Description
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified

Personal history

ICD-10-CM	Description
Z85.028	Personal history of other malignant neoplasm of stomach

Examples of head and neck cancer ICD-10-CM codes⁶

Head and neck cancer sites

ICD-10-CM	Description
C06.9	Malignant neoplasm of mouth, unspecified
C07	Malignant neoplasm of parotid gland
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C08.9	Malignant neoplasm of major salivary gland, unspecified

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

Serious adverse reactions occurred in 19% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were vomiting, ILD, pneumonia, pyrexia, and urinary tract infection. Fatalities due to adverse reactions occurred in 0.8% of patients including COVID-19 and sudden death (1 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%), decreased blood potassium (35%), constipation (34%), musculoskeletal pain (31%), diarrhea (29%), decreased appetite (29%), headache (22%), respiratory infection (22%), abdominal pain (21%), increased blood bilirubin (20%), and stomatitis (20%).

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Examples of primary non-small cell lung cancer ICD-10-CM codes⁶

Primary lung cancer sites

ICD-10-CM	Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C7A.1	Malignant poorly differentiated neuroendocrine tumors

Personal history

ICD-10-CM	Description
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z92.21	Personal history of antineoplastic chemotherapy
Z92.3	Personal history of irradiation

Important Safety Information (cont'd)

Adverse Reactions(cont'd)

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.

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.

Please see additional Important Safety Information throughout, and see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

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





Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement

Access

Affordability

Coding & Reimbursement

Distribution

Important Safety Information

Examples of primary ovarian cancer ICD-10-CM codes⁶

Ovarian cancer sites

ICD-10-CM	Description
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified

Genetic susceptibility

ICD-10-CM	Description
Z15.02	Genetic susceptibility to malignant neoplasm of ovary

Personal history

ICD-10-CM	Description
Z85.43	Personal history of malignant neoplasm of ovary
Z92.22	Personal history of monoclonal drug therapy

Important Safety Information (cont'd)

Adverse Reactions(cont'd)

The most common ($\geq 20\%$) 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%).

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Coding & Reimbursement

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Access

Affordability

Coding & Reimbursement

Distribution

Important Safety Information

Examples of primary pancreatic cancer ICD-10-CM codes⁶

Pancreatic cancer sites

ICD-10-CM	Description
C24.1	Malignant neoplasm of ampulla of Vater
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified

Personal history

ICD-10-CM	Description
Z85.07	Personal history of malignant neoplasm of pancreas

Estrogen and Other Hormones & Growth Factor Receptors¹

Z17.31*	Human epidermal growth factor receptor 2 positive status
Z17.32*	Human epidermal growth factor receptor 2 negative status**
Z17.410*	Hormone receptor positive with human epidermal growth factor receptor 2 positive status
Z17.411*	Hormone receptor positive with human epidermal growth factor receptor 2 negative status**
Z17.420*	Hormone receptor negative with human epidermal growth factor receptor 2 positive status

*Code appropriate diagnosis from the C50.

HER2-negative (IHC 0, IHC1+ or IHC2+/ISH-) breast cancer includes both HER2-low, defined as IHC 1+ or IHC 2+/ISH-, and HER2 ultra-low, defined as IHC 0 with some membrane staining.

Important Safety Information (cont'd)

Adverse Reactions(cont'd)

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%).

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Coding & Reimbursement

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Examples of metastatic cancer ICD-10-CM codes⁶

The codes listed below represent common sites to which metastatic breast cancer, metastatic non-small cell lung cancer, and metastatic gastric or gastroesophageal junction adenocarcinoma metastasize. There may be other metastatic sites as well. These codes are for example only.

Metastasis to lymph nodes

ICD-10-CM	Description
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C77.1	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
C77.2	Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
C77.3	Secondary and unspecified malignant neoplasm of axilla and upper limb lymph nodes
C77.4	Secondary and unspecified malignant neoplasm of inguinal and lower limb lymph nodes
C77.5	Secondary and unspecified malignant neoplasm of intrapelvic lymph nodes
C77.8	Secondary and unspecified malignant neoplasm of lymph nodes of multiple regions
C77.9	Secondary and unspecified malignant neoplasm of lymph node, unspecified

Metastasis to liver

ICD-10-CM	Description
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct

Metastasis to spleen, pancreas, and other digestive organs

ICD-10-CM	Description
C78.4	Secondary malignant neoplasm of small intestine
C78.5	Secondary malignant neoplasm of large intestine and rectum
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.80	Secondary malignant neoplasm of unspecified digestive organ
C78.89	Secondary malignant neoplasm of other digestive organs

Important Safety Information (cont'd)

Adverse Reactions(cont'd)

HER2-Mutant Unresectable or Metastatic NSCLC (5.4 mg/kg)

DESTINY-Lung02 evaluated 2 dose levels (5.4 mg/kg [n=101] and 6.4 mg/kg [n=50]); however, only the results for the recommended dose of 5.4 mg/kg intravenously every 3 weeks are described below due to increased toxicity observed with the higher dose in patients with NSCLC, including ILD/pneumonitis.

The safety of ENHERTU was evaluated in 101 patients with HER2-mutant unresectable or metastatic NSCLC who received ENHERTU 5.4 mg/kg intravenously once every 3 weeks until disease progression or unacceptable toxicity in DESTINY-Lung02. The median duration of treatment was 8 months (range: 0.7 to 28) for patients who received ENHERTU.

Serious adverse reactions occurred in 40% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, pleural effusion, thrombocytopenia, dyspnea, nausea, pneumonia, vomiting, myocarditis, pulmonary embolism, and increased troponin I. Fatalities due to adverse reactions occurred in 3% of patients including ILD/pneumonitis, cerebrovascular accident, and pneumococcal sepsis (1 patient each).

ENHERTU was permanently discontinued in 17% of patients. Adverse reactions which resulted in permanent discontinuation of ENHERTU were ILD/pneumonitis, pneumonia, blood bilirubin increased, hypokalemia, metastases to meninges, and myocarditis. Dose interruptions of ENHERTU due to adverse reactions occurred in 50% of patients. Adverse reactions which required dose interruption (>2%) included neutropenia, COVID-19, ILD/pneumonitis, fatigue, anemia, and pneumonia. Dose reductions due to an adverse reaction occurred in 20% of patients. The most frequent adverse reactions (>2%) associated with dose reduction were neutropenia, fatigue, and decreased appetite.

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Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement

Examples of metastatic cancer ICD-10-CM codes⁶ (cont'd)

Metastasis to lungs and pleura

ICD-10-CM	Description
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.1	Secondary malignant neoplasm of mediastinum
C78.2	Secondary malignant neoplasm of pleura
C78.30	Secondary malignant neoplasm of unspecified respiratory organ
C78.39	Secondary malignant neoplasm of other respiratory organs

Metastasis to brain

ICD-10-CM	Description
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges

Metastasis to bone and bone marrow

ICD-10-CM	Description
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow

Important Safety Information (cont'd)

Adverse Reactions(cont'd)

The most common ($\geq 20\%$) adverse reactions, including laboratory abnormalities, were decreased hemoglobin (68%), nausea (67%), decreased white blood cell count (66%), decreased neutrophil count (59%), decreased lymphocyte count (56%), increased aspartate aminotransferase (51%), decreased albumin (50%), decreased platelet count (49%), fatigue (48%), increased alanine aminotransferase (41%), decreased appetite (41%), constipation (38%), increased alkaline phosphatase (37%), vomiting (32%), decreased blood potassium (29%), diarrhea (24%), alopecia (22%), and musculoskeletal pain (21%).

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

The safety of ENHERTU was evaluated in 187 patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma in DESTINY-Gastric01. Patients intravenously received at least 1 dose of either ENHERTU (N=125) 6.4 mg/kg every 3 weeks or either irinotecan (N=55) 150 mg/m² biweekly or paclitaxel (N=7) 80 mg/m² weekly for 3 weeks. The median duration of treatment was 4.6 months (range: 0.7 to 22.3) for patients who received ENHERTU.

Serious adverse reactions occurred in 44% of patients receiving ENHERTU 6.4 mg/kg. Serious adverse reactions in $>2\%$ of patients who received ENHERTU were decreased appetite, ILD, anemia, dehydration, pneumonia, cholestatic jaundice, pyrexia, and tumor hemorrhage. Fatalities due to adverse reactions occurred in 2.4% of patients: disseminated intravascular coagulation, large intestine perforation, and pneumonia occurred in 1 patient each (0.8%).

ENHERTU was permanently discontinued in 15% of patients, of which ILD accounted for 6%. Dose interruptions due to adverse reactions occurred in 62% of patients treated with ENHERTU. The most frequent adverse reactions ($>2\%$) associated with dose interruption were neutropenia, anemia, decreased appetite, leukopenia, fatigue, thrombocytopenia, ILD, pneumonia, lymphopenia, upper respiratory tract infection, diarrhea, and decreased blood potassium. Dose reductions occurred in 32% of patients treated with ENHERTU. The most frequent adverse reactions ($>2\%$) associated with dose reduction were neutropenia, decreased appetite, fatigue, nausea, and febrile neutropenia.

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Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement

Example of a completed CMS-1500 claim form for an ENHERTU-treated patient

Prescribers use this form when billing insurers for medication administered in the physician's office and for their professional services.

HEALTH INSURANCE CLAIM FORM
APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12

1. MEDICARE ☒ MEDICAID ☐ TRICARE ☐ CHAMPVA ☐ GROUP HEALTH PLAN ☒ FECA ☐ OTHER ☐ 1a. INSURED'S I.D. NUMBER (For Program in Item 1)
12345678

2. PATIENT'S NAME (Last Name, First Name, Middle Initial)
Smith, Karen A.

3. PATIENT'S BIRTH DATE MM/DD/YY **MM: 03 DD: 14 YY: 49** SEX ☒ F ☐ M

4. INSURED'S NAME (Last Name, First Name, Middle Initial)
Smith, Karen A.

5. PATIENT'S ADDRESS (No., Street)
123 Main St.

6. PATIENT RELATIONSHIP TO INSURED
Self ☒ Spouse ☐ Child ☐ Other ☐

7. INSURED'S ADDRESS (No., Street)
123 Main St.

8. RESERVED FOR NUCC USE

9. OTHER INSURED'S NAME (Last Name, First Name, Middle Initial)
10001

10. IS PATIENT'S CONDITION RELATED TO:
a. OTHER INSURED'S POLICY OR GROUP NUMBER
b. RESERVED FOR NUCC USE
c. RESERVED FOR NUCC USE
d. INSURANCE PLAN NAME OR PROGRAM NAME

11. INSURED'S POLICY GROUP OR FECA NUMBER
10001

12. IS THERE ANOTHER HEALTH BENEFIT PLAN?
☐ YES ☒ NO If yes, complete items 9, 9a, and 9d.

13. INSURED'S OR AUTHORIZED PERSON'S SIGNATURE I authorize payment of medical benefits to the undersigned physician or supplier for services described below.
SIGNED **Karen Smith** DATE **07/01/2020**

14. DATE OF CURRENT ILLNESS, INJURY, OR PREGNANCY (LMP)
MM/DD/YY **07/01/2020** QUAL **QUAL**

15. OTHER DATE MM/DD/YY

16. DATES PATIENT UNABLE TO WORK IN CURRENT OCCUPATION
FROM MM/DD/YY TO MM/DD/YY

17. NAME OF REFERRING PROVIDER OR OTHER SOURCE
17a. NPI **17b. NPI**

18. HOSPITALIZATION DATES RELATED TO CURRENT SERVICES
FROM MM/DD/YY TO MM/DD/YY

19. ADDITIONAL CLAIM INFORMATION (Designated by NUCC)

20. OUTSIDE LAB? ☒ YES ☐ NO \$ CHARGES

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind. **1**
A. **07 01 20 07 01 20 11 J9358**
B. **07 01 20 07 01 20 11 96413**
C. **07 01 20 07 01 20 11 J9358 JW**
D. **07 01 20 07 01 20 11**
E. **07 01 20 07 01 20 11**
F. **07 01 20 07 01 20 11**
G. **07 01 20 07 01 20 11**
H. **07 01 20 07 01 20 11**
I. **07 01 20 07 01 20 11**
J. **07 01 20 07 01 20 11**
K. **07 01 20 07 01 20 11**
L. **07 01 20 07 01 20 11**

22. RESUBMISSION CODE **1** ORIGINAL REF. NO. **1**

23. PRIOR AUTHORIZATION NUMBER **1**

24. A. DATE(S) OF SERVICE From MM/DD/YY To MM/DD/YY B. PLACE OF SERVICE EMG C. D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS MODIFIER
1 **07 01 20 07 01 20 11 J9358**
2 **07 01 20 07 01 20 11 96413**
3 **07 01 20 07 01 20 11 J9358 JW**
4
5
6

25. FEDERAL TAX I.D. NUMBER **12345** SSN EIN **12345**

26. PATIENT'S ACCOUNT NO. **12345**

27. ACCEPT ASSIGNMENT? (For gov. claims, see back) ☒ YES ☐ NO

28. TOTAL CHARGE \$ **12345**

29. AMOUNT PAID \$ **12345**

30. Rsvd for NUCC Use

31. SIGNATURE OF PHYSICIAN OR SUPPLIER INCLUDING DEGREE OR CREDENTIALS (I certify that the statements on the reverse apply to this bill and are made a part thereof.)
SIGNED **John Doe MD** DATE **07/01/20**

32. SERVICE FACILITY LOCATION INFORMATION
**Oncology Specialists of Springfield
123 Main St. Springfield Anytown USA**

33. BILLING PROVIDER INFO & PH # **12345**

34. BILLING PROVIDER INFO & PH # **12345**

35. BILLING PROVIDER INFO & PH # **12345**

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100. BILLING PROVIDER INFO & PH # **12345**

NUCC Instruction Manual available at: www.nucc.org PLEASE PRINT OR TYPE APPROVED OMB-0938-1197 FORM 1500 (02-12)

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Input Diagnosis Code(s) here

Complete Sections E-J

Important Safety Information (cont'd)

Adverse Reactions(cont'd)

The most common ($\geq 20\%$) adverse reactions, including laboratory abnormalities, were decreased hemoglobin (75%), decreased white blood cell count (74%), decreased neutrophil count (72%), decreased lymphocyte count (70%), decreased platelet count (68%), nausea (63%), decreased appetite (60%), increased aspartate aminotransferase (58%), fatigue (55%), increased blood alkaline phosphatase (54%), increased alanine aminotransferase (47%), diarrhea (32%), decreased blood potassium (30%), vomiting (26%), constipation (24%), increased blood bilirubin (24%), pyrexia (24%), and alopecia (22%).

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ENHERTU
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20 mg/mL INJECTION FOR INTRAVENOUS USE

4U



Coding & Reimbursement

Coding, appeals, and denial support is available to help with reimbursement

Example of a completed UB-04 claim form for an ENHERTU-treated patient

Hospitals use this form when billing insurers for medication administered in the inpatient or outpatient setting. Please include the appropriate revenue codes when billing in the outpatient setting.

1		2		3a PAT CMT #		4 STATE OF BILL	
				b MED REQ #		131	
5 FID TAX NO.		6 STATEMENT COVERED PERIOD FROM		7 THROUGH			
12345678		07/01/2020		07/01/2020			
8 PATIENT NAME		a Karen Smith		9 PATIENT ADDRESS		a 123 Main St.	
b New York		c NY		d 10001		e	
10 BIRTHDATE		11 SEX		12 DATE		13 ADMISSION	
03/19/1949		F		07/01/2020		14 TYPE	
15 SMC		16 DHR		17 STATE		18	
19		20		21		22	
23		24		25		26	
27		28		29		30	
31 OCCURRENCE DATE		32 CODE		33 OCCURRENCE DATE		34 CODE	
35 OCCURRENCE DATE		36 CODE		37 OCCURRENCE DATE		38 CODE	
39 VALUE CODES		40 VALUE CODES		41 VALUE CODES		42	
AMOUNT		AMOUNT		AMOUNT			
a		b		c		d	
43 REV CD		44 HPCS / RATE / HPPS CODE		45 SERV DATE		46 SERV UNITS	
0636		J9358					
47 TOTAL CHARGES		48 NON-COVERED CHARGES		49			
0335		96413					
43 DESCRIPTION		44 HPCS / RATE / HPPS CODE		45 SERV DATE		46 SERV UNITS	
Drugs requiring detailed coding (Pharmacy extension series 063X)							
Rad-Chemo IV							
PAGE		OF		CREATION DATE		TOTALS	
50 PAYER NAME		51 HEALTH PLAN ID		52 PRIOR PAYMENTS		53 EST. AMOUNT DUE	
Medicare		1234567890					
54 INSURED'S NAME		55 INSURED'S UNIQUE ID		56 GROUP NAME		57 INSURANCE GROUP NO.	
Karen Smith		123456789					
58 TREATMENT AUTHORIZATION CODES		59 DOCUMENT CONTROL NUMBER		60 EMPLOYER NAME			
61 ADMIT DATE		62 PATIENT REASON FOR		63 PRIOR CODE		64 ICD	
74 PRINCIPAL PROCEDURE CODE		75 OTHER PROCEDURE CODE		76 ATTENDING		77 QUAL	
				LAST		FIRST	
78 OTHER PROCEDURE CODE		79 OTHER PROCEDURE CODE		76 OTHER		77 QUAL	
				LAST		FIRST	
80 REMARKS		81 CPT		78 OTHER		79 QUAL	
				LAST		FIRST	
				79 OTHER		80 QUAL	
				LAST		FIRST	
UB-04 CMS-1450		APPROVED CMS NO.		THE CERTIFICATIONS ON THE REVERSE APPLY TO THIS BILL AND ARE MADE A PART HEREOF		NUBC	

Input Diagnosis Code(s) here

Important Safety Information (cont'd) Adverse Reactions(cont'd)

HER2-Positive (IHC 3+) Unresectable or Metastatic Solid Tumors

The safety of ENHERTU was evaluated in 347 adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who received ENHERTU 5.4 mg/kg intravenously once every 3 weeks in DESTINY-Breast01, DESTINY-PanTumor02, DESTINY-Lung01, and DESTINY-CRC02. The median duration of treatment was 8.3 months (range 0.7 to 30.2).

Serious adverse reactions occurred in 34% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were sepsis, pneumonia, vomiting, urinary tract infection, abdominal pain, nausea, pneumonitis, pleural effusion, hemorrhage, COVID-19, fatigue, acute kidney injury, anemia, cellulitis, and dyspnea. Fatalities due to adverse reactions occurred in 6.3% of patients including ILD/pneumonitis (2.3%), cardiac arrest (0.6%), COVID-19 (0.6%), and sepsis (0.6%). The following events occurred in 1 patient each (0.3%): acute kidney injury, cerebrovascular accident, general physical health deterioration, pneumonia, and hemorrhagic shock.

Please see additional Important Safety Information throughout, and see full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

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





Distribution

Connect with select Specialty Distributors and Specialty Pharmacy Providers

Specialty Distributors

ENHERTU will primarily be distributed through Specialty Distributors via the buy-and-bill process

Specialty Distributor	Phone number	Fax number	Website
ASD Healthcare	1-800-746-6273	1-800-547-9413	www.asdhealthcare.com
BioCare	1-800-304-3064	1-602-850-6215	https://biocare-us.com/
Cardinal Health Specialty Distribution	1-855-855-0708	1-614-553-6301	https://specialtyonline.cardinalhealth.com/
CuraScript SD	1-877-599-7748	1-800-862-6208	www.curascriptsd.com
Dakota Drug, Inc.	1-866-210-5887	1-763-421-0661	www.dakdrug.com
DMS Pharmaceutical	1-877-788-1100	1-847-518-1105	www.dmspharma.com
McKesson Plasma and Biologics	1-877-625-2566	1-888-752-7626	www.mckesson.com/Pharmaceutical-Distribution/Plasma-Biologics
McKesson Specialty Health	1-800-482-6700	1-800-289-9285	https://mckessonspecialtyhealth.com/
Morris & Dickson Specialty Distribution	1-800-388-3833	1-318-798-5237	www.morrisdickson.com/products/specialty
Oncology Supply	1-800-633-7555	1-800-248-8205	www.oncologysupply.com

Important Safety Information (cont'd)

Adverse Reactions(cont'd)

ENHERTU was permanently discontinued in 15% of patients, of which ILD/pneumonitis accounted for 10%. Dose interruptions due to adverse reactions occurred in 48% of patients. The most frequent adverse reactions (>2%) associated with dose interruption were decreased neutrophil count, anemia, COVID-19, fatigue, decreased white blood cell count, and ILD/pneumonitis. Dose reductions occurred in 27% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were fatigue, nausea, decreased neutrophil count, ILD/pneumonitis, and diarrhea.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased white blood cell count (75%), nausea (69%), decreased hemoglobin (67%), decreased neutrophil count (66%), fatigue (59%), decreased lymphocyte count (58%), decreased platelet count (51%), increased aspartate aminotransferase (45%), increased alanine aminotransferase (44%), increased blood alkaline phosphatase (36%), vomiting (35%), decreased appetite (34%), alopecia (34%), diarrhea (31%), decreased blood potassium (29%), constipation (28%), decreased sodium (22%), stomatitis (20%), and upper respiratory tract infection (20%).

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Access

Affordability

Coding & Reimbursement

Distribution

Important Safety Information



Distribution

Connect with select Specialty Distributors and Specialty Pharmacy Providers

ENHERTU may be dispensed through specialty pharmacy providers

ENHERTU4U specialists can identify your Specialty Pharmacy Provider options.

If you prefer, you and your staff can also work directly with the Specialty Pharmacy Providers if:

- You have already identified the Specialty Pharmacy Provider that is in your patient's network
- You currently use a Specialty Pharmacy Provider that is in your patient's network

The specialty distribution model will cover 98% of all hospital and health systems and 99% of all community oncology utilization.

Important Safety Information (cont'd)

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:** *ENHERTU as Monotherapy:* 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%). Of the 125 patients with HER2-positive locally advanced or metastatic gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg in DESTINY-Gastric01, 56% were ≥65 years and 14% were ≥75 years. No overall differences in efficacy or safety were observed between patients ≥65 years of age compared to younger patients. *ENHERTU in Combination with Pertuzumab:* In patients with HER2-positive unresectable or metastatic breast cancer treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), 17% were ≥65 years and 3% were ≥75 years. No overall differences in efficacy or safety were observed between patients ≥65 years compared to younger patients. *ENHERTU followed by THP:* Of the 320 patients with HER2-positive early breast cancer treated with ENHERTU 5.4 mg/kg followed by THP, 12% were ≥65 years and 1.6% were ≥75 years. No overall differences in efficacy were observed between patients ≥65 years compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients ≥65 years (38%) as compared to younger patients (30%).
- **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).

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Important Safety Information

Important Safety Information Indications

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

- HER2-Positive Early Breast Cancer
 - As neoadjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) Stage II or III breast cancer, as determined by an FDA-authorized test followed by a taxane, trastuzumab, and pertuzumab (THP)
 - As adjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) breast cancer who have residual invasive disease following neoadjuvant trastuzumab (with or without pertuzumab) and taxane-based treatment
- HER2-Positive Metastatic Breast Cancer
 - In combination with pertuzumab as first-line treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH+) breast cancer, as determined by an FDA-authorized test
 - As monotherapy for the treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH+) 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 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
- HER2-Mutant Unresectable or Metastatic Non-Small Cell Lung Cancer (NSCLC)
 - As monotherapy for the treatment of adult patients with unresectable or metastatic NSCLC whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-authorized test, and who have received a prior systemic therapy
This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- HER2-Positive Locally Advanced or Metastatic Gastric Cancer
 - As monotherapy for the treatment of adult patients with locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen
- HER2-Positive (IHC 3+) Unresectable or Metastatic Solid Tumors
 - As monotherapy for the treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options
This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

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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. In the adjuvant HER2+ breast cancer setting, if drug-induced ILD is suspected, rule out radiotherapy-related pneumonitis. If only radiotherapy-related pneumonitis is suspected, consider interruption of ENHERTU for Grade 2 and permanently discontinue ENHERTU for Grade ≥3.

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+) (5.4 mg/kg)

ENHERTU as Monotherapy

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.

ENHERTU in Combination with Pertuzumab

In patients treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), ILD occurred in 12% of patients. Median time to first onset was 8.0 months (range: 0.6 to 33.8). Fatal outcomes due to ILD and/or pneumonitis occurred in 0.5% of patients treated with ENHERTU in combination with pertuzumab.

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, ILD occurred in 4.4% of patients. Median time to first onset was 2.7 months (range: 1.1 to 6.0). Fatal outcomes due to ILD and/or pneumonitis occurred in 1 patient (0.3%) treated with ENHERTU followed by THP.

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, ILD occurred in 10% of patients. Median time to first onset was 2.8 months (range: 1.2 to 21).

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Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

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 $0.5 \times 10^9/L$), interrupt ENHERTU until resolved to Grade 2 or less, then maintain dose. For Grade 4 neutropenia (ANC $<0.5 \times 10^9/L$), interrupt ENHERTU until resolved to Grade 2 or less, then reduce dose by 1 level. For febrile neutropenia (ANC $<1.0 \times 10^9/L$ and temperature $>38.3^\circ C$ or a sustained temperature of $\geq 38^\circ C$ for more than 1 hour), interrupt ENHERTU until resolved, then reduce dose by 1 level.

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+) (5.4 mg/kg)

ENHERTU as Monotherapy

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.

ENHERTU in Combination with Pertuzumab

In patients treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), decreased neutrophil count occurred in 79% of patients. Median time to first onset was 22 days (range: 5 to 994). Twenty-nine percent had Grade 3 or 4 decreased neutrophil count. Febrile neutropenia was reported in 2.6% of patients.

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, a decrease in neutrophil count was reported in 58% of patients. Seventeen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 42 days (range: 11 to 165). Febrile neutropenia was reported in 0.9% of patients.

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, a decrease in neutrophil count was reported in 72% of patients. Fifty-one percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 16 days (range: 4 to 187). Febrile neutropenia was reported in 4.8% 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.

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+) (5.4 mg/kg)

ENHERTU as Monotherapy

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.

ENHERTU in Combination with Pertuzumab

In patients treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), LVEF decrease was reported in 11% of patients, of which 2.1% were Grade 3 or 4.

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, LVD was reported in 1.3% of patients, of which 0.3% were Grade 3.

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, no clinical adverse events of heart failure were reported; however, on echocardiography, 8% were found to have asymptomatic Grade 2 decrease in LVEF.

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

Adverse Reactions

HER2-Positive, HER2-Low, and HER2-Ultralow Breast Cancer, HER2-Mutant NSCLC, and Solid Tumors (Including IHC 3+) (5.4 mg/kg)

ENHERTU as Monotherapy

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, DESTINY-Lung01, DESTINY-Lung02, DESTINY-CRC02, and DESTINY-PanTumor02. Among these patients, 67% were exposed for >6 months and 39% were exposed for >1 year. In this pooled safety population, the most common ($\geq 20\%$) 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%).

ENHERTU in Combination with Pertuzumab

The pooled safety population reflects exposure to ENHERTU 5.4 mg/kg in combination with pertuzumab intravenously every 3 weeks in 431 patients in DESTINY-Breast07 (n=50), and DESTINY-Breast09 (n=381). Among these patients, 86% were exposed for >6 months and 73% were exposed for >1 year. In this pooled safety population, the most common ($\geq 20\%$) adverse reactions, including laboratory

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Important Safety Information (cont'd)

Adverse Reactions (cont'd)

abnormalities, were decreased white blood cell count (86%), decreased hemoglobin (80%), decreased neutrophil count (79%), nausea (74%), increased alanine aminotransferase (65%), diarrhea (64%), increased aspartate aminotransferase (63%), decreased lymphocyte count (61%), decreased platelet count (55%), increased blood alkaline phosphatase (54%), decreased blood potassium (54%), fatigue (53%), alopecia (48%), vomiting (46%), upper respiratory tract infection (32%), constipation (31%), decreased appetite (31%), decreased weight (28%), musculoskeletal pain (23%), increased blood bilirubin (23%), and abdominal pain (22%).

HER2-Positive Early Breast Cancer

DESTINY-Breast11

The safety of ENHERTU followed by THP was evaluated in 320 patients with HER2-positive (IHC 3+ or ISH+) early breast cancer who received at least 1 dose of ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11. ENHERTU was administered by intravenous infusion once every three weeks for 4 cycles followed by THP for 4 cycles. The median duration of treatment was 5.6 months (range: 0.7 to 9.1) for patients who received ENHERTU followed by THP.

Serious adverse reactions occurred in 11% of patients receiving ENHERTU followed by THP, including COVID-19 (0.9%) and ILD/pneumonitis (0.6%). Fatal adverse reactions occurred in 0.6% of patients, including ILD/pneumonitis and death not otherwise specified (1 patient each).

In patients treated with ENHERTU followed by THP, the permanent discontinuation of ENHERTU due to adverse reactions occurred in 1.3%, of which ILD/pneumonitis accounted for 0.6%. Dose interruptions of ENHERTU due to adverse reactions occurred in 11% of patients. The most frequent adverse reactions (>2%) associated with dose interruption were decreased neutrophil count and COVID-19. Dose reductions of ENHERTU occurred in 2.5% of patients treated with ENHERTU.

The most common (≥20%) adverse reactions in patients treated with ENHERTU followed by THP, including laboratory abnormalities, were decreased hemoglobin (83%), increased alanine aminotransferase (79%), increased aspartate aminotransferase (74%), decreased white blood cell count (67%), nausea (65%), peripheral neuropathy (59%), diarrhea (59%), decreased neutrophil count (58%), alopecia (48%), fatigue (41%), decreased lymphocyte count (40%), rash (31%), musculoskeletal pain (30%), decreased blood potassium (29%), constipation (29%), vomiting (29%), stomatitis (23%), and decreased appetite (20%).

DESTINY-Breast05

The safety of ENHERTU was evaluated in 806 patients with HER2-positive breast cancer with residual invasive disease following neoadjuvant HER2-targeted therapy who then received at least one dose of ENHERTU 5.4 mg/kg. ENHERTU was administered by intravenous infusion once every three weeks for 14 cycles. The median duration of treatment was 10 months (range: 0.7 to 16) for patients who received ENHERTU.

Serious adverse reactions occurred in 17% of patients receiving ENHERTU. Serious adverse reactions in ≥1% of patients who received ENHERTU were ILD/pneumonitis, radiation pneumonitis, pneumonia, and platelet count decreased. Fatal adverse reactions occurred in 0.4% of patients including ILD/pneumonitis (2 patients) and respiratory tract infection (1 patient).

Permanent discontinuation of ENHERTU due to an adverse reaction occurred in 18% of patients. The adverse reaction which resulted in permanent discontinuation of ENHERTU >2% included ILD/pneumonitis. Dose interruptions of ENHERTU due to an adverse reaction occurred in 50% of patients. Adverse reactions which required dosage interruptions in >2% included radiation pneumonitis, neutrophil count decreased, COVID-19, white blood cell count decreased, ILD/pneumonitis, platelet count decreased, upper respiratory tract infection, fatigue, cough, and

pyrexia. Dose reductions of ENHERTU due to an adverse reaction occurred in 26% of patients. Adverse reactions which required dose reductions in >2% of patients included nausea, fatigue, platelet count decreased, ILD/pneumonitis, and neutrophil count decreased.

The most common (≥20%) adverse reactions, including laboratory abnormalities, in patients receiving ENHERTU were decreased white blood cell count (80%), decreased lymphocyte count (72%), decreased neutrophil count (72%), nausea (71%), decreased hemoglobin (61%), increased aspartate aminotransferase (60%), fatigue (54%), increased alanine aminotransferase (53%), decreased platelet count (46%), increased blood alkaline phosphatase (39%), constipation (32%), vomiting (31%), decreased blood potassium (27%), diarrhea (23%), musculoskeletal pain (23%), and decreased appetite (20%).

ILD was reported in 17% of patients receiving ENHERTU, which included COVID-19 pneumonia, interstitial lung disease, lung opacity, organizing pneumonia, pneumocystis jirovecii pneumonia, pneumonia, and pneumonitis which was adjudicated as ILD (irrespective of causality). Adjudicated drug-related ILD for ENHERTU was 10% for all Grades and 0.9% for Grades 3 or 4.

HER2-Positive Metastatic Breast Cancer

DESTINY-Breast09

The safety of ENHERTU 5.4 mg/kg in combination with pertuzumab was evaluated in DESTINY-Breast09, a randomized, three-arm, multicenter study including 763 patients with HER2-positive (IHC 3+ or ISH+) unresectable or metastatic breast cancer. Three hundred eighty-one patients received ENHERTU in combination with pertuzumab and 382 patients received THP (taxane [docetaxel or paclitaxel], trastuzumab, and pertuzumab). Among patients who received ENHERTU in combination with pertuzumab, the median duration of treatment was 22 months (range: 0.3 months to 44.5 months).

Serious adverse reactions occurred in 27% of patients receiving ENHERTU in combination with pertuzumab. Serious adverse reactions in >1% of patients were diarrhea, pneumonia, febrile neutropenia, hypokalemia, vomiting, ILD, pulmonary embolism, and sepsis. Fatalities due to adverse reactions occurred in 3.4% of patients including pneumonia (n=3), ILD (n=2), sepsis (n=2), pulmonary embolism, septic shock, acute kidney injury, dyspnea, febrile neutropenia, and intestinal ischemia (1 patient each).

ENHERTU was discontinued for adverse reactions in 21% of patients. The most frequent adverse reaction (>2%) associated with permanent discontinuation was ILD/pneumonitis (6%). Dose interruptions due to adverse reactions occurred in 69% of patients. The most frequent adverse reactions (>2%) associated with dose interruption were COVID-19, neutropenia, upper respiratory tract infection, fatigue, anemia, hypokalemia, ILD/pneumonitis, thrombocytopenia, pneumonia, diarrhea, transaminase increased, leukopenia, cough, pyrexia, decreased appetite, and blood bilirubin increased. Dose reductions occurred in 46% of patients treated with ENHERTU in combination with pertuzumab. The most frequent adverse reactions (>2%) associated with dose reduction were fatigue, neutropenia, nausea, diarrhea, ILD/pneumonitis, thrombocytopenia, vomiting, transaminases increased, decreased weight, febrile neutropenia, and hypokalemia.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased white blood cell count (87%), decreased hemoglobin (80%), decreased neutrophil count (78%), nausea (75%), increased alanine aminotransferase (66%), diarrhea (64%), increased aspartate aminotransferase (62%), decreased lymphocyte count (62%), decreased platelet count (56%), increased blood alkaline phosphatase (55%), decreased blood potassium (54%), fatigue (53%), alopecia (48%), vomiting (46%), upper respiratory tract infection (33%), constipation (33%), decreased appetite (32%), decreased weight (30%), COVID-19 (28%), musculoskeletal pain (24%), increased blood bilirubin (23%), and abdominal pain (23%).

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Important Safety Information (cont'd)

Adverse Reactions (cont'd)

DESTINY-Breast03

The safety of ENHERTU was evaluated in 257 patients with unresectable or metastatic HER2-positive breast cancer who received at least 1 dose of ENHERTU 5.4 mg/kg intravenously once every 3 weeks in DESTINY-Breast03. The median duration of treatment was 14 months (range: 0.7 to 30) for patients who received ENHERTU.

Serious adverse reactions occurred in 19% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were vomiting, ILD, pneumonia, pyrexia, and urinary tract infection. Fatalities due to adverse reactions occurred in 0.8% of patients including COVID-19 and sudden death (1 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%), decreased blood potassium (35%), constipation (34%), musculoskeletal pain (31%), diarrhea (29%), decreased appetite (29%), headache (22%), respiratory infection (22%), abdominal pain (21%), increased blood bilirubin (20%), and stomatitis (20%).

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.

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%).

HER2-Mutant Unresectable or Metastatic NSCLC (5.4 mg/kg)

DESTINY-Lung02 evaluated 2 dose levels (5.4 mg/kg [n=101] and 6.4 mg/kg [n=50]); however, only the results for the recommended dose of 5.4 mg/kg intravenously every 3 weeks are described below due to increased toxicity observed with the higher dose in patients with NSCLC, including ILD/pneumonitis.

The safety of ENHERTU was evaluated in 101 patients with HER2-mutant unresectable or metastatic NSCLC who received ENHERTU 5.4 mg/kg intravenously once every 3 weeks until disease progression or unacceptable toxicity in DESTINY-Lung02. The median duration of treatment was 8 months (range: 0.7 to 28) for patients who received ENHERTU.

Serious adverse reactions occurred in 40% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, pleural effusion, thrombocytopenia, dyspnea, nausea, pneumonia, vomiting, myocarditis, pulmonary embolism, and increased troponin I. Fatalities due to adverse reactions occurred in 3% of patients including ILD/pneumonitis, cerebrovascular accident, and pneumococcal sepsis (1 patient each).

ENHERTU was permanently discontinued in 17% of patients. Adverse reactions which resulted in permanent discontinuation of ENHERTU were ILD/pneumonitis, pneumonia, blood bilirubin increased, hypokalemia, metastases to meninges, and myocarditis. Dose interruptions of ENHERTU due to adverse reactions occurred in 50% of patients. Adverse reactions which required dose interruption (>2%) included neutropenia, COVID-19, ILD/pneumonitis, fatigue, anemia, and pneumonia. Dose reductions due to an adverse reaction occurred in 20% of patients. The most frequent adverse reactions (>2%) associated

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Important Safety Information (cont'd)

Adverse Reactions (cont'd)

with dose reduction were neutropenia, fatigue, and decreased appetite.

The most common ($\geq 20\%$) adverse reactions, including laboratory abnormalities, were decreased hemoglobin (68%), nausea (67%), decreased white blood cell count (66%), decreased neutrophil count (59%), decreased lymphocyte count (56%), increased aspartate aminotransferase (51%), decreased albumin (50%), decreased platelet count (49%), fatigue (48%), increased alanine aminotransferase (41%), decreased appetite (41%), constipation (38%), increased alkaline phosphatase (37%), vomiting (32%), decreased blood potassium (29%), diarrhea (24%), alopecia (22%), and musculoskeletal pain (21%).

HER2-Positive Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

The safety of ENHERTU was evaluated in 187 patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma in DESTINY-Gastric01. Patients intravenously received at least 1 dose of either ENHERTU (N=125) 6.4 mg/kg every 3 weeks or either irinotecan (N=55) 150 mg/m² biweekly or paclitaxel (N=7) 80 mg/m² weekly for 3 weeks. The median duration of treatment was 4.6 months (range: 0.7 to 22.3) for patients who received ENHERTU.

Serious adverse reactions occurred in 44% of patients receiving ENHERTU 6.4 mg/kg. Serious adverse reactions in $>2\%$ of patients who received ENHERTU were decreased appetite, ILD, anemia, dehydration, pneumonia, cholestatic jaundice, pyrexia, and tumor hemorrhage. Fatalities due to adverse reactions occurred in 2.4% of patients: disseminated intravascular coagulation, large intestine perforation, and pneumonia occurred in 1 patient each (0.8%).

ENHERTU was permanently discontinued in 15% of patients, of which ILD accounted for 6%. Dose interruptions due to adverse reactions occurred in 62% of patients treated with ENHERTU. The most frequent adverse reactions ($>2\%$) associated with dose interruption were neutropenia, anemia, decreased appetite, leukopenia, fatigue, thrombocytopenia, ILD, pneumonia, lymphopenia, upper respiratory tract infection, diarrhea, and decreased blood potassium. Dose reductions occurred in 32% of patients treated with ENHERTU. The most frequent adverse reactions ($>2\%$) associated with dose reduction were neutropenia, decreased appetite, fatigue, nausea, and febrile neutropenia.

The most common ($\geq 20\%$) adverse reactions, including laboratory abnormalities, were decreased hemoglobin (75%), decreased white blood cell count (74%), decreased neutrophil count (72%), decreased lymphocyte count (70%), decreased platelet count (68%), nausea (63%), decreased appetite (60%), increased aspartate aminotransferase (58%), fatigue (55%), increased blood alkaline phosphatase (54%), increased alanine aminotransferase (47%), diarrhea (32%), decreased blood potassium (30%), vomiting (26%), constipation (24%), increased blood bilirubin (24%), pyrexia (24%), and alopecia (22%).

HER2-Positive (IHC 3+) Unresectable or Metastatic Solid Tumors

The safety of ENHERTU was evaluated in 347 adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who received ENHERTU 5.4 mg/kg intravenously once every 3 weeks in DESTINY-Breast01, DESTINY-PanTumor02, DESTINY-Lung01, and DESTINY-CRC02. The median duration of treatment was 8.3 months (range 0.7 to 30.2).

Serious adverse reactions occurred in 34% of patients receiving ENHERTU. Serious adverse reactions in $>1\%$ of patients who received ENHERTU were sepsis, pneumonia, vomiting, urinary tract infection, abdominal pain, nausea, pneumonitis, pleural effusion, hemorrhage, COVID-19, fatigue, acute kidney injury, anemia, cellulitis, and dyspnea. Fatalities due to adverse reactions occurred in 6.3% of patients including ILD/pneumonitis (2.3%), cardiac arrest (0.6%), COVID-19 (0.6%), and sepsis (0.6%). The following events occurred in 1 patient each (0.3%): acute kidney injury, cerebrovascular accident, general physical health deterioration, pneumonia, and hemorrhagic shock.

ENHERTU was permanently discontinued in 15% of patients, of which ILD/pneumonitis accounted for 10%. Dose interruptions due to adverse reactions occurred in 48% of patients. The most frequent adverse reactions ($>2\%$) associated with dose interruption were decreased neutrophil count, anemia, COVID-19, fatigue, decreased white blood cell count, and ILD/pneumonitis. Dose reductions occurred in 27% of patients treated with ENHERTU. The most frequent adverse reactions ($>2\%$) associated with dose reduction were fatigue, nausea, decreased neutrophil count, ILD/pneumonitis, and diarrhea.

The most common ($\geq 20\%$) adverse reactions, including laboratory abnormalities, were decreased white blood cell count (75%), nausea (69%), decreased hemoglobin (67%), decreased neutrophil count (66%), fatigue (59%), decreased lymphocyte count (58%), decreased platelet count (51%), increased aspartate aminotransferase (45%), increased alanine aminotransferase (44%), increased blood alkaline phosphatase (36%), vomiting (35%), decreased appetite (34%), alopecia (34%), diarrhea (31%), decreased blood potassium (29%), constipation (28%), decreased sodium (22%), stomatitis (20%), and upper respiratory tract infection (20%).

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:** *ENHERTU as Monotherapy:* 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%). Of the 125 patients with HER2-positive locally advanced or metastatic gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg in DESTINY-Gastric01, 56% were ≥ 65 years and 14% were ≥ 75 years. No overall differences in efficacy or safety were observed between patients ≥ 65 years of age compared to younger patients. *ENHERTU in Combination with Pertuzumab:* In patients with HER2-positive unresectable or metastatic breast cancer treated with ENHERTU 5.4 mg/kg in combination with pertuzumab (N=431), 17% were ≥ 65 years and 3% were ≥ 75 years. No overall differences in efficacy or safety were observed between patients ≥ 65 years compared to younger patients. *ENHERTU followed by THP:* Of the 320 patients with HER2-positive early breast cancer treated with ENHERTU 5.4 mg/kg followed by THP, 12% were ≥ 65 years and 1.6% were ≥ 75 years. No overall differences in efficacy were observed between patients ≥ 65 years compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients ≥ 65 years (38%) as compared to younger patients (30%).

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Important Safety Information (cont'd)

Use in Specific Populations (cont'd)

- **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.

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