

for certain adults with **HER2-positive** metastatic breast cancer (mBC) who have received a prior anti-HER2 breast cancer treatment

Metastatic is defined as cancer that has spread to other parts of the body. HER2, human epidermal growth factor receptor 2.

Not an actual patient.

What is ENHERTU?

ENHERTU is a prescription medicine used to treat adults who have human epidermal growth factor receptor 2 (HER2)-positive breast cancer that cannot be removed by surgery or that has spread to other parts of the body (metastatic), and who have received a prior anti-HER2 breast cancer treatment:

- for metastatic disease. or
- have breast cancer that has come back during or within 6 months of completing treatment for their early-stage breast cancer.

It is not known if ENHERTU is safe and effective in children.

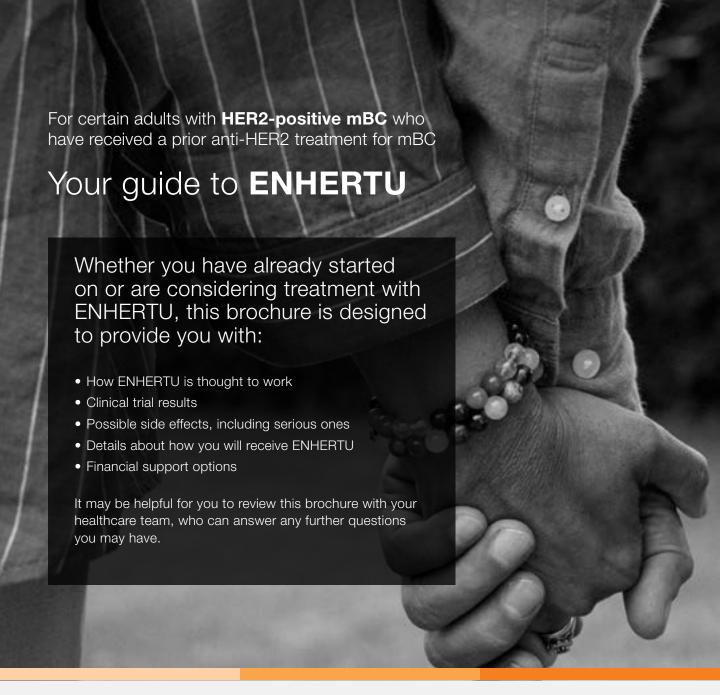
IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ENHERTU?

ENHERTU can cause serious side effects, including:

• Lung problems that may be severe, lifethreatening or that may lead to death. If you develop lung problems your healthcare provider may treat you with corticosteroid medicines. Tell your healthcare provider right away if you get any of the following signs and symptoms: • Cough • Trouble breathing or shortness of breath • Fever • Other new or worsening breathing symptoms (such as chest tightness, wheezing)





• Low white blood cell count (neutropenia). Low white blood cell counts are common with ENHERTU and can sometimes be severe. Your healthcare provider will check your white blood cell counts before starting ENHERTU and before starting each dose. Tell your healthcare provider right away if you develop any signs or symptoms of an infection or have fever or chills during treatment with ENHERTU.

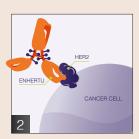


How is ENHERTU thought to work?

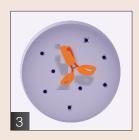
As a targeted treatment called an antibody-drug conjugate (ADC), ENHERTU is designed to work differently than traditional chemotherapies.



ENHERTU is made up of an antibody with the chemotherapy attached



The antibody part of ENHERTU targets and attaches to HER2 on the cancer cell



ENHERTU enters the cancer cell and the chemotherapy is released



The chemotherapy part of ENHERTU helps destroy the cancer cell as well as other cells nearby

Although ENHERTU is designed to target HER2 on cancer cells, it may affect some healthy cells.

ENHERTU may not work for everyone.

IMPORTANT SAFETY INFORMATION (cont'd)

- Heart problems that may affect your heart's ability to pump blood. Your healthcare provider will check your heart function before starting treatment with ENHERTU. Tell your healthcare provider right away if you get any of the following signs and symptoms: New or worsening shortness of breath
- Coughing Feeling tired Swelling of your ankles or legs Irregular heartbeat Sudden weight gain
- Dizziness or feeling light-headed Loss of consciousness





Your healthcare provider will check you for these side effects during your treatment with ENHERTU. Your healthcare provider may reduce your dose, delay treatment or completely stop treatment with ENHERTU if you have severe side effects.



How was ENHERTU studied in HER2-positive mBC?

ENHERTU was compared to adotrastuzumab emtansine in a clinical study of 524 people who:

- Had HER2-positive breast cancer that had spread to other parts of their body or could not be removed by surgery, and
- Had received a prior treatment for HER2-positive metastatic breast cancer (mBC) or had cancer come back during or within 6 months of treatment after surgery

In this trial, 261 people were treated with ENHERTU and 263 were treated with adotrastuzumab emtansine.

ENHERTU was studied in many types of adults, including those with:



Different ages*



Various hormone receptor (HR) statuses



Tumors that had spread (metastasized) to other parts of the body, including the liver, lungs, and bones



Tumors that had spread to the brain and were stable

IMPORTANT SAFETY INFORMATION (cont'd)

- Harm to your unborn baby. Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ENHERTU.
 - If you are able to become pregnant, your healthcare provider should do a pregnancy test before you start treatment with ENHERTU.
 - **Females** who are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for 7 months after the last dose.
 - **Males** who have female partners that are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for 4 months after the last dose.



^{*}Patients studied were 20 to 83 years of age.

Progression-free survival

Initial results (May 2021)

With ENHERTU, people lived longer without their cancer growing or spreading

compared to ado-trastuzumab emtansine

Compared to ado-trastuzumab emtansine, people who received ENHERTU were:

72% more likely

to be alive without their cancer progressing

This is called median progression-free survival. A median is the middle number in a set of numbers. Median progression-free survival (mPFS) measures the amount of time that half of the people enrolled in the study were on treatment before their cancer started growing or spreading.

At the time of data analysis, median progression-free survival was not yet reached for people receiving ENHERTU. This means that more than half of people receiving ENHERTU were alive without their cancer growing or spreading. This compares to half of the people receiving ado-trastuzumab emtansine who reached median progression-free survival at about 7 months before their cancer began to grow or spread.

• 67% (174 of 261) of people treated with ENHERTU were alive at the time of data analysis without their cancer progressing, compared to 40% (105 of 263) of people treated with ado-trastuzumab emtansine

IMPORTANT SAFETY INFORMATION (cont'd)

Before you receive ENHERTU, tell your healthcare provider about all of your medical conditions, including if you:

- Have lung or breathing problems.
- Have signs or symptoms of an infection.
- Have or have had any heart problems.
- Are breastfeeding or plan to breastfeed. It is not known if ENHERTU passes into your breast milk. Do not breastfeed during treatment with ENHERTU and for 7 months after the last dose.



Overall survival

Initial results (May 2021)

In the first assessment, overall survival results were not available

Follow-up results (July 2022)

People receiving ENHERTU lived longer

compared with people receiving adotrastuzumab emtansine

- At the time of updated data analysis, more than 50% of people receiving ENHERTU or adotrastuzumab emtansine were still alive*
- ENHERTU reduced the risk of death in patients by 36% vs ado-trastuzumab emtansine
- 65% (170 of 261) of people treated with ENHERTU were alive at the time of this data analysis (median follow-up was 28.4 months), and 52% (138 of 263) of people treated with ado-trastuzumab emtansine were alive at the time of data analysis (median follow-up was 26.5 months)

Updated results (November 2023)

Median overall survival with ENHERTU

and ado-trastuzumab emtansine[†]

• 52.6 months with ENHERTU and 42.7 months with ado-trastuzumab emtansine

This is called median overall survival. A median is the middle number in a set of numbers. Median overall survival is the length of time, from either the day of diagnosis or the start of treatment, that half the patients in a group are still alive.

*At the time of data analysis, since more than 50% of people receiving ENHERTU or ado-trastuzumab emtansine were still alive, the results could not be reported in months.

[†]These study results were based on an exploratory analysis, which was not intended to compare the two treatments. The study was also open-label, meaning that both the patients and trial investigators knew which treatment patients received. Therefore, the results could have been influenced by people switching to another treatment, leaving the study, or other factors. This means the results of the exploratory analysis cannot be fully explained and may not be the effect of the treatment. Each person's experience may differ. Speak with your doctor about what you may expect.

IMPORTANT SAFETY INFORMATION (cont'd)

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive ENHERTU?

- You will receive ENHERTU into your vein through an intravenous (IV) line by your healthcare provider.
- ENHERTU is given 1 time every three weeks (21-day treatment cycle).



Response to treatment

Initial results (May 2021)

In the first assessment, more people had their tumors shrink with ENHERTU than with ado-trastuzumab emtansine*†

Overall response



&



This is called overall response rate. Overall response rate is the proportion of patients who have a partial or complete response to therapy.

Of the people who responded to ENHERTU:

- 16% (39 of 248) of people achieved a complete response with ENHERTU and 8% (20 of 241) of people with ado-trastuzumab emtansine. A complete response means the tumor could not be seen on imaging tests
- 67% (166 of 248) of people achieved a partial response with ENHERTU and 28% (67 of 241) of people with ado-trastuzumab emtansine. A partial response means the tumor shrank by at least 30%

*These study results were based on an exploratory analysis, which was not intended to compare the two treatments. The study was also open-label, meaning that both the patients and trial investigators knew which treatment patients received. Therefore, the results could have been influenced by people switching to another treatment, leaving the study, or other factors. This means the results of the exploratory analysis cannot be fully explained and may not be the effect of the treatment. Each person's experience may differ. Speak with your doctor about what you may expect. *Based on the people in the first assessment with measurable disease (248 people who received ENHERTU and 241 people who received ado-trastuzumab emtansine). In the first assessment, 83% (205 of 248) of people had their tumors shrink with ENHERTU and 36% (87 of 241) of people with ado-trastuzumab emtansine.

IMPORTANT SAFETY INFORMATION (cont'd)

How will I receive ENHERTU? (cont'd)

- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will give you medicines before your infusion to help prevent nausea and vomiting.
- Your healthcare provider may slow down or temporarily stop your infusion of ENHERTU if you have an infusion-related reaction, or permanently stop ENHERTU if you have severe infusion reactions.
- If you miss a planned dose of ENHERTU, call your healthcare provider right away to schedule an appointment. Do not wait until the next planned treatment cycle.



Response to treatment (cont'd)

Updated results (July 2022)*

- 82% of people had their tumors shrink with ENHERTU
- 37% of people had their tumors shrink with ado-trastuzumab emtansine

Of the people who responded to ENHERTU in the updated assessment:

- 21% (52 of 246) of people achieved a complete response with ENHERTU and 9% (21 of 240) of people treated with ado-trastuzumab emtansine
- 61% (150 of 246) of people achieved a partial response with ENHERTU and 28% (67 of 240) of people treated with ado-trastuzumab emtansine

*Based on the people in the updated assessment with measurable disease (246 people who received ENHERTU and 240 people who received ado-trastuzumab emtansine). In the updated assessment, 82% (202 of 246) of people had their tumors shrink with ENHERTU and 37% (88 of 240) of people with ado-trastuzumab emtansine.

IMPORTANT SAFETY INFORMATION (cont'd)

What are the possible side effects of ENHERTU?

ENHERTU can cause serious side effects. See "What is the most important information I should know about ENHERTU?"

The most common side effects of ENHERTU when used at the 5.4 mg/kg dose include:

- Low white blood cell counts
- Nausea
- Low red blood cell counts
- Feeling tired
- Low platelet counts
- Increased liver function tests
- Vomiting

- Hair loss
- Constipation
- Low levels of blood potassium
- Decreased appetite
- Diarrhea
- Muscle or bone pain



Additional results with ENHERTU

Initial results (May 2021)

Disease control

In the first assessment, 98% (242 of 248) of people treated with ENHERTU had their tumors respond to treatment in at least one of the following ways:



This is called disease control rate. The disease control rate is the percentage of patients who have achieved complete response, partial response, or stable disease.*

*Not tested for statistical significance and not designed to show differences between treatments. Statistical significance describes a mathematical measure of difference between groups. The difference is statistically significant if it is greater than what might be expected to happen by chance alone.

IMPORTANT SAFETY INFORMATION (cont'd)

What are the possible side effects of ENHERTU? (cont'd)

ENHERTU may cause fertility problems in males, which may affect the ability to father children. Talk to your healthcare provider if you have concerns about fertility.





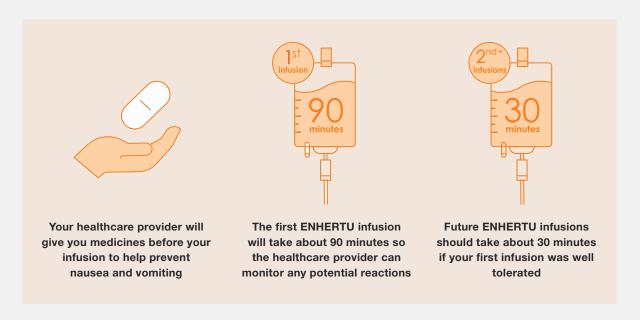
What are the possible side effects of ENHERTU? (cont'd)

These are not all of the possible side effects of ENHERTU. Call your doctor for medical advice about side effects. You may report side effects to Daiichi Sankyo at 1-877-437-7763 or to FDA at 1-800-FDA-1088.



How will I receive ENHERTU?

ENHERTU is given as an intravenous (IV) infusion. You will receive an ENHERTU infusion once every 3 weeks, either at your oncologist's office or at a nearby infusion center.



If you miss a planned dose of ENHERTU, call your healthcare provider right away to schedule an appointment. Do not wait until the next planned treatment cycle.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about ENHERTU?

ENHERTU can cause serious side effects, including:

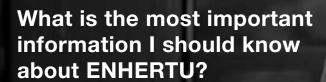
• Lung problems that may be severe, life-threatening or that may lead to death. If you develop lung problems your healthcare provider may treat you with corticosteroid medicines. Tell your healthcare provider right away if you get any of the following signs and symptoms: • Cough • Trouble breathing or shortness of breath • Fever • Other new or worsening breathing symptoms (such as chest tightness, wheezing)





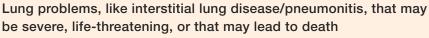
• Low white blood cell count (neutropenia). Low white blood cell counts are common with ENHERTU and can sometimes be severe. Your healthcare provider will check your white blood cell counts before starting ENHERTU and before starting each dose. Tell your healthcare provider right away if you develop any signs or symptoms of an infection or have fever or chills during treatment with ENHERTU.





ENHERTU can cause serious side effects. Some serious or life-threatening side effects may affect your lungs, heart, or white blood cell count, affecting your ability to fight infection.

Pay special attention to new or worsening symptoms as they may be related to:



Call or see your healthcare provider right away if you develop any of the following signs and symptoms or if these symptoms get worse:

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

If lung problems develop, your healthcare provider may treat you with corticosteroid medicines.

Low white blood cell count (neutropenia)

- Low white blood cell counts are common with ENHERTU and can sometimes be severe
- Your healthcare provider will check your white blood cell counts before starting ENHERTU and before starting each dose
- Tell your healthcare provider right away if you develop any signs or symptoms of an infection or have fever or chills during treatment with ENHERTU

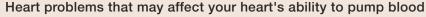
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Not actual patients.





What is the most important information I should know about ENHERTU? (cont'd)



Your healthcare provider will check your heart function before starting treatment with ENHERTU. Tell your healthcare provider right away if you get any of the following signs and symptoms:

- New or worsening shortness of breath
- Coughing
- Feeling tired
- Swelling of your ankles or legs
- Irregular heartbeat
- Sudden weight gain
- Dizziness or feeling light-headed
- Loss of consciousness

Your healthcare provider will check you for these side effects during your treatment with ENHERTU. Your healthcare provider may reduce your dose, delay treatment, or completely stop treatment with ENHERTU if you have severe side effects.

Harm to your unborn baby

Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ENHERTU.



- If you are able to become pregnant, your healthcare provider should do a pregnancy test before you start treatment with ENHERTU
- Females who are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for 7 months after the last dose
- Males who have female partners that are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for 4 months after the last dose

These are not all of the possible side effects of ENHERTU. Call your doctor for medical advice about side effects.



During treatment with ENHERTU, side effects may occur and you should notify your healthcare provider as early as possible

The most common side effects of ENHERTU when used at the 5.4 mg/kg dose include:

- · Low white blood cell counts
- Nausea
- Low red blood cell counts
- · Feeling tired
- Low platelet counts
- Increased liver function tests
- Vomiting

- Hair loss
- Constipation
- Low levels of blood potassium
- Decreased appetite
- Diarrhea
- Muscle or bone pain

The majority of side effects in people receiving ENHERTU were mild or moderate*; however, some people may have serious side effects that could lead to death. It is important to call your doctor for medical advice about side effects.

*Mild side effects are side effects you may have but they show no outward signs or medical intervention may not be needed. Moderate side effects may require some medical intervention or may affect you as you do day-to-day activities.



These are not all the possible side effects of ENHERTU. Call your doctor for medical advice about side effects. You are encouraged to report side effects of ENHERTU by calling **1-877-437-7763**. If you prefer to report these to the FDA, visit www.FDA.gov/medwatch or call **1-800-FDA-1088** (1-800-332-1088).

Useful tips may help you manage side effects. To learn more, visit ENHERTU.com/mBC/safety



Support for you

What are some ways **ENHERTU4U** may be able to help after I've been prescribed **ENHERTU**?

The ENHERTU4U program is designed to help you access and afford your prescribed ENHERTU treatment, including benefits reviews, prior authorization and/or claims appeal information, and paying for your prescription.*



ACCESS

ENHERTU4U is here to help your healthcare provider understand your insurance company's requirements for access to treatment with ENHERTU.



FINANCIAL ASSISTANCE

We have multiple options to help you afford your treatment.* Your healthcare provider can provide more information about how ENHERTU4U may be able to help.

For more information about **ENHERTU4U**, please call **1-833-ENHERTU** (**1-833-364-3788**) or scan the QR code to visit **ENHERTU4U.com**.



ENHERTU4U does not guarantee access or cost savings for patients prescribed ENHERTU.



^{*}For eligible patients. Terms and conditions apply.





Connect with helpful resources



American Cancer Society cancer.org



Living Beyond Breast Cancer Ibbc.org



METAvivor metavivor.org



Share Cancer Support sharecancersupport.org



Susan G. Komen komen.org

This is not an all-inclusive list of resources.

For more information about your **ENHERTU** treatment, talk to your healthcare provider and visit **ENHERTU.com/resources**.



IMPORTANT SAFETY INFORMATION

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Before you receive ENHERTU, tell your healthcare provider about all of your medical conditions, including if you:

- Have lung or breathing problems.
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- Are breastfeeding or plan to breastfeed. It is not known if ENHERTU passes into your breast milk.
 Do not breastfeed during treatment with ENHERTU and for 7 months after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.



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- You will receive ENHERTU into your vein through an intravenous (IV) line by your healthcare provider.
- ENHERTU is given 1 time every three weeks (21-day treatment cycle).
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- Low levels of blood potassium
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- Muscle or bone pain

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What is ENHERTU?

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- for metastatic disease, or
- have breast cancer that has come back during or within 6 months of completing treatment for their early-stage breast cancer.

It is not known if ENHERTU is safe and effective in children.





Not actual patients.

References: 1. ENHERTU. Prescribing information. Daiichi Sankyo, Inc.; 2024. 2. Ogitani Y, Aida T, Hagihara K, et al. DS-8201a, a novel HER2-targeting ADC with a novel DNA topoisomerase I inhibitor, demonstrates a promising antitumor efficacy with differentiation from T-DM1. Clin Cancer Res. 2016;22(20):5097-5108.

3. Nakada T, Sugihara K, Jikoh T, Abe Y, Agatsuma T. The latest research and development into the antibody—drug conjugate, [fam-] trastuzumab deruxtecan (DS-8201a), for HER2 cancer therapy. Chem Pharm Bull (Tokyo). 2019;67(3):173-185.

4. Hurvitz SA, Hegg R, Chung WP, et al. Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial. Lancet. 2023;401(10371):105-117.

5. Hurvitz SA, Hegg R, Chung WP, et al. Supplement to: Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial. Lancet. 2023;401(10371):105-117.

6. Cortés J, Kim SB, Chung WP, et al; DESTINY-Breast03 Trial Investigators. Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer. N Engl J Med. 2022;386(12):1143-1154.

7. Data on file. Daiichi Sankyo, Inc. Basking Ridge, NJ.

8. ENHERTU. Medication Guide. Daiichi Sankyo, Inc. 2024.

9. National Cancer Institute, National Institutes of Health, US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0. Published November 27, 2017.

Please see full Important Safety Information on pages 20-23, and <u>click here for full ENHERTU</u>

<u>Prescribing Information</u>, including Boxed WARNINGS, and <u>click here for Medication Guide</u>.







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