ENHERTU®
trastuzumab deruxtecan

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HCP Guide

AstraZeneca

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Health Care Professional Guide

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ENHERTU®

(Trastuzumab deruxtecan)

Important Risk Minimisation Information on ILD/Pneumonitis with Treatment of ENHERTU (Trastuzumab deruxtecan)

This Health Care Professional (HCP) Guide is

- provided for HCPs to read before prescribing and administering ENHERTU.
- an important tool to ensure the early recognition and diagnosis of ILD/pneumonitis, to allow prompt and appropriate treatment and minimise serious outcomes.
- a reminder to distribute a Patient Card to any patient receiving ENHERTU treatment for the first time or if asked for a new copy.

Not all possible side effects are listed in this Guide.
Please read the ENHERTU product label for full details including Posology and Warnings and Special Precautions for use.

What is ENHERTU?

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate.
ENHERTU as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens.
ENHERTU is indicated for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen.

What is Interstitial Lung Disease (ILD)/Pneumonitis?

ILD is a broad term for a group of diffuse, parenchymal lung disorders that present as nonspecific cough, fever, and shortness of breath (dyspnoea), including pneumonitis and idiopathic pulmonary fibrosis (unknown cause).

Risk of ILD/Pneumonitis with ENHERTU

In clinical studies, of the 234 patients with unresectable or metastatic HER2-positive breast cancer treated with ENHERTU, ILD occurred in 9% of patients. Fatal outcomes due to ILD and/or pneumonitis occurred in 2.6% of patients treated with ENHERTU. Median time to first onset was 4.1 months (range: 1.2 to 8.3).

Identification and minimisation of ILD/Pneumonitis

Early diagnosis and appropriate management of events of ILD/pneumonitis are essential to minimise serious outcomes. Patients should be monitored closely, and management initiated at the first suspicion of ILD/pneumonitis (e.g. cough, shortness of breath, fever, or other new or worsening breathing problems).

Investigating suspected ILD/Pneumonitis

Any evidence of ILD/pneumonitis should be promptly investigated and managed with the goal of suppressing inflammation and preventing irreversible fibrosis with potentially fatal outcome.
For Suspected ILD/Pneumonitis[2,3]

- Consider further evaluations, which could include:
  - Radiographic imaging (e.g. high-resolution CT)
  - Pulmonologist consultation (infectious disease consultation as clinically indicated)
  - Bronchoscopy and bronchoalveolar lavage if clinically indicated and feasible
  - Pulmonary function tests and pulse oximetry (SpO_2)
  - Clinical laboratory tests
    - > Arterial blood gases, if clinically indicated
    - > Blood culture, blood cell count, differential WBC count, CRP, markers associated with interstitial pneumonia (KL-6, SP-A, SP-D)
- Diagnosis of ILD requires exclusion of other causes. If the Adverse Event is confirmed to have an etiology other than ENHERTU-related ILD/pneumonitis, follow routine clinical practice
- If another etiology for the Adverse Event cannot be identified and it could be related to ENHERTU, then follow the ILD/pneumonitis management guidance as outlined in section 'Instructions for Management of Suspected ENHERTU related ILD/Pneumonitis'.

Instructions for Management of Suspected ENHERTU related ILD/Pneumonitis:

CTCAE Grade	Description	Treatment Modification
Grade 1	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Interrupt ENHERTU until the event resolves to Grade 0 then: • if resolved in 28 days or less from date of onset, maintain dose. • if resolved in greater than 28 days from date of onset, reduce dose one level (e.g. First dose reduction: 4.4 mg/kg) • Consider corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g. ≥0.5 mg/kg/day prednisolone or equivalent)
Grade 2	Symptomatic; medical intervention indicated; limiting instrumental activities of daily living	Permanently discontinue ENHERTU • Promptly initiate corticosteroid treatment (e.g. ≥1 mg/kg/day prednisolone or equivalent) as soon as ILD/ pneumonitis is suspected for at least 14 days or until complete resolution of clinical symptoms and chest computed tomography (CT) findings. • Then gradually taper for at least 4 weeks.
Grade 3	Severe symptoms; limiting self-care activities of daily living; oxygen indicated	
Grade 4	Life-threatening respiratory compromise; urgent intervention indicated (e.g. tracheotomy or intubation)	
Grade 5	Death	

Grading based on the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE)[1]

General Risk Factors Linked to ILD/Pneumonitis related to other drugs

The exact mechanisms via which ENHERTU may cause ILD are not yet known.[4] General risk factors for the development of drug-induced ILD vary according to the disease, drug, and population being considered and include the following.[5,6,7]

- **Patient history of ILD or lung disease:** preexisting lung disease and reduced lung function are important risk factors for drug-induced ILD[8,9,10,11]
- **Poor overall health:** in oncology, poor performance status or metastatic disease may increase the risk for drug-induced ILD[12]
- **Smoking status:** smokers are at an increased risk for drug induced ILD[10]
- **Advanced age:** the elderly, especially those over 60 years old, may have a significantly higher risk for drug-induced ILD[9,10,11]
- **Ethnicity:** Japanese or African American patients may be at an increased risk for drug-induced ILD[9,13]
- **Male sex:** men may be at an increased risk for drug-induced ILD[10,11]
- **Prior treatment**: prior chemotherapy, treatment with multiple chemotherapy regimens, thoracic radiotherapy, and combination therapy with multiple molecular targeted agents with or without cytotoxic agents may increase a patient's risk for drug-induced ILD[9,10,12]

References

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8. Sakurada T, Kakiuchi S, Tajima S, et al. Characteristics of and risk factors for interstitial lung disease induced by chemotherapy for lung cancer. Ann Pharmacother. 2015;49(4):398-404.
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Talking points for Patient's Visit (First or Following)

At the first visit (before prescribing ENHERTU):

- Inform the patient that they may experience serious and potentially fatal side effects of lung problems.
- Check whether the patient has a history of ILD/pneumonitis or a history of lung comorbidities, history of corticosteroids treatment.
- Check for signs and symptoms of lung problems.
- Inform the patient that early diagnosis and appropriate management of events of ILD/pneumonitis are essential to minimise serious outcomes.
- Instruct the patient to contact you immediately if they experience even mild signs or symptoms (e.g. cough, dyspnoea, fever, and/or any new or worsening respiratory symptoms), as some events can worsen rapidly if not treated.
- Instruct the patient not to treat their own symptoms.
- Provide the patient with the Patient Card and discuss the therapy with the patient before starting treatment with ENHERTU.
- Always fill in the Patient Card and remind the patient to carry it.

At all visits:

- Check for signs and symptoms of lung problems.
- Remind the patient that early diagnosis and appropriate management of lung problems are essential to minimise life-threatening complications.
- Remind the patient of the importance of adhering to scheduled appointments.

Potential questions to ask your patients to help with early identification of ILD/Pneumonitis:

- Have you been coughing recently? Is it a dry cough?
- Have you had any shortness of breath, especially during or after physical activity?
- Have you experienced any new breathing or respiratory problems?
- If you already have respiratory problems, have they become worse?
- Have you had a fever?
- Have you been feeling tired?
- Do you smoke or use e-cigarettes?

Reporting suspected adverse drug reactions (ADRs)

Where to find further information
ENHERTU® physician leaflet
You can also contact us on phone number: 073-2226099
To order additional educational materials please call: 073-2226099
Or email to: Safety.Israel@astrazeneca.com

To report suspected adverse reaction
please contact AstraZeneca at:
https://www.contactazmedical.astrazeneca.com
or
Safety.Israel@astrazeneca.com
You can also call us on phone number: 073-2226099
You may also report side effects to the Israeli ministry of health
by using online form: WWW.HEALTH.GOV.IL
or by entering the link: https://sideeffects.health.gov.il

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