swissmedic

Summary report on authorisation dated 31 January 2025

Enhertu® (active substance: trastuzumab deruxtecan)

Indication extension in Switzerland: 6 March 2023

Infusion for the second-line treatment of adults with inoperable or metastatic HER2-low breast cancer

About the medicinal product

Enhertu contains the active substance trastuzumab deruxtecan and is used to treat adult patients with HER2-low breast cancer. This means that the tumour has only small amounts of the HER2 protein. HER2 is the abbreviation for human epidermal growth factor receptor 2. These receptors trigger division of cancer cells. The medicine is suitable for patients whose breast cancer cannot be operated on or has already formed metastases, on condition that the patient has previously received chemotherapy for metastatic breast cancer or that the cancer has returned during or within 6 months of completing supportive chemotherapy.

Patients with hormone-sensitive breast cancer must also have previously received hormone therapy that either did not work or they were unable to tolerate.

Breast cancer is the most common type of cancer in women and the main cause of cancer-related deaths in women. If the cancer has already metastasised, the disease is considered incurable and the 5-year survival rate is only around 25%.

A specific feature of some breast cancer tumours is the protein HER2, which is present in high amounts in about 20% of patients (HER2-positive breast cancer). Thanks to modern medicines that target HER2, the prognosis has improved significantly.

However, approximately 55% of all breast cancer patients have tumours that contain only small amounts of HER2 (HER2-low breast cancer). To date, there are no specific HER2-targeted treatment guidelines for this group, and they are treated like patients whose tumours do not have HER2. Treatment for HER2-low breast cancer depends on whether the tumour has other hormone receptors (HR).

This indication extension for Enhertu was authorised in connection with "Project Orbis". Project Orbis is a programme for promising cancer treatments coordinated by the FDA, the US regulatory authority. It provides a framework for the concurrent submission and review of cancer medicines by several international partner authorities in various countries. The ultimate aim is to give patients faster access to innovative cancer

treatments. Currently, the authorisation authorities in Australia (TGA), Brazil (ANVISA), Canada (HC), Israel (MOH), Singapore (HSA), Switzerland (Swissmedic) and the United Kingdom (MHRA) are represented in Project Orbis.

The medicinal product Enhertu has already been authorised by Swissmedic for 2 other indications.

Mode of action

Enhertu contains the active substance trastuzumab deruxtecan. This active substance combines an antibody (a protein) that can recognise and bind to the HER2 receptor on breast cancer cells with a substance known as a topoisomerase I inhibitor, which is effective against malignant tumours. As a result, the genetic material of the tumour cells is damaged, leading to the death of the cancer cells.

Use

Enhertu is a prescription-only medicine and is authorised as a single-dose vial containing 100 mg trastuzumab deruxtecan powder. The powder is dissolved in sterile water, diluted with glucose solution, and administered slowly via a vein.
The recommend dose is 5.4 mg/kg body weight every 3 weeks. The first dose should be administered as a 90-minute infusion. If the previous infusion was well tolerated, the duration of the infusion can be shortened to 30 minutes. Treatment is continued until further progression of the disease or until unacceptable side effects occur.

Efficacy

The efficacy of Enhertu was investigated in the DESTINY-Breast04 study in 557 adult patients with inoperable or metastatic HER2-low breast cancer who had previously received chemotherapy for metastatic breast cancer or whose cancer had returned during or within 6 months of completing adjuvant chemotherapy. Patients were treated with either Enhertu (5.4 mg/kg every 3 weeks) or chemotherapy of the physician's choice. Patients were differentiated according to whether their breast cancer expressed hormone receptors (HR-positive) or not. Progression-free survival[1] (PFS) was assessed, which was evaluated by a blinded independent central review (BICR). In the HR-positive patients, results showed a significant improvement in PFS in the Enhertu group, with a median[2] PFS of 10.1 months, compared to 5.4 months in the chemotherapy group. Results in the general population showed a significant improvement in PFS in the Enhertu group, with a median PFS of 9.9 months, compared to 5.1 months in the chemotherapy group. Overall survival[3] (OS) in HR-positive patients was also improved, with a median OS of 23.9 months in the Enhertu group versus 17.5 months in the chemotherapy group.

[1] Progression-free survival (PFS): period between the start of a treatment or a clinical trial and the onset of disease progression or the death of the patient.

[2] Median: the value that lies exactly in the middle of a distribution of data is called the median or central value. Half of the data values are always less than the median, the other half are always greater.

[3] Overall survival (OS): refers to the period between the start of treatment and the death of the patient.

Precautions, undesirable effects, & risks

While undergoing treatment with Enhertu, there is a risk of lung disease (interstitial lung disease, ILD) that can be potentially fatal. Patients should be monitored for respiratory symptoms. The most common undesirable effects are nausea, fatigue, vomiting, decreased appetite, diarrhoea, anaemia, neutropenia (lack of specific immune cells), and hair loss. All precautions, risks, and other possible undesirable effects are listed in the Information for healthcare professionals.

Why the medicinal product has been authorised

There is currently no specific medicinal treatment for patients with HER2-low breast cancer after they have received prior chemotherapy. Enhertu offers a new treatment option for these patients. The clinical study showed that Enhertu significantly slows disease progression and improves patient survival compared to conventional chemotherapy. Despite a number of undesirable effects, the safety profile of Enhertu can be easily managed. Based on all the available data, the benefits of Enhertu outweigh the risks if used correctly in appropriately selected patients. Swissmedic has therefore extended the authorisation of the medicinal product Enhertu, containing the active substance trastuzumab deruxtecan, in Switzerland.

Further information on the medicinal product

Information for healthcare professionals: Information for healthcare professionals, Enhertu®

Healthcare professionals can answer any further questions.

The date of revision of this text corresponds to that of the SwissPAR. New information concerning the authorised medicinal product in question will not be incorporated into the Summary report on authorisation.

Swissmedic monitors medicinal products authorised in Switzerland. Swissmedic initiates the necessary action in the event of newly discovered adverse drug reactions or other safety-relevant signals. New findings that could impair the quality, efficacy, or safety of this medicinal product are recorded and published by Swissmedic. If necessary, the medicinal product information is adapted.