swissmedic

Summary report on authorisation dated 17 January 2025

Enhertu® (active substance: trastuzumab deruxtecan)

Temporary authorisation extension in Switzerland: 8 May 2024

Infusion for the treatment of locally advanced or metastatic HER2-positive gastric or gastro-oesophageal junction adenocarcinoma in adults

About the medicinal product

Enhertu, containing the active substance trastuzumab deruxtecan, is a medicine for the treatment of adults with locally advanced or metastatic HER2-positive gastric or gastro-oesophageal junction[1] adenocarcinoma[2]. Enhertu is used in patients who have already received other HER2-based treatments, but who have not responded to prior treatments or whose disease has progressed.

HER2 is the abbreviation for human epidermal growth factor receptor 2. These receptors trigger division of cancer cells. Around 20% of patients experience elevated levels of HER2. Specific targeted treatments are available for these patients.

Swissmedic has already authorised Enhertu for 3 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 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 recommended dose is 6.4 mg/kg body weight administered

[1] Gastro-oesophageal junction (GEJ): point where the oesophagus joins the stomach.

[2] Adenocarcinoma is a malignant tumour of the glands, in this case the glands in the stomach and the junction between the oesophagus and stomach

once 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.

Efficacy

Enhertu was investigated in 2 clinical trials – DESTINY-Gastric02 and DESTINY-Gastric01. In the DESTINY-Gastric02 trial, 79 patients with locally advanced or metastatic HER2-positive gastric or gastro-oesophageal junction cancer who had already been treated with trastuzumab received Enhertu as an intravenous infusion every 3 weeks. The confirmed[3] objective response rate (ORR)[4] for the trial was 41.8% and the median[5] duration of response (DOR)[6] was 8.1 months. There was no comparator group in this trial.

In the DESTINY-Gastric01 trial, 126 patients were treated with Enhertu and compared with 62 patients who received the physician's choice of chemotherapy. The confirmed ORR for this trial was 39.7% for the Enhertu group, compared with 11.3% for the chemotherapy group. Median overall survival (OS) was 12.5 months for Enhertu and 8.9 months for the chemotherapy group. The DESTINY-Gastric01 trial only enrolled patients from Asia who had previously been treated with at least 2 lines of therapy.

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. Other very common adverse reactions after administration of Enhertu are infections and diseases of the respiratory tract, changes in blood cell counts, nausea, fatigue, decreased appetite, vomiting, constipation, and diarrhoea. 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 a major need for treatment options for patients with locally advanced or metastatic HER2-positive gastric or gastro-oesophageal junction adenocarcinoma who have already received a first-line standard therapy. The prognosis for patients whose disease progresses after first-line treatment is poor. Despite the available treatment options, there is a need to improve therapy outcomes in these patients.

A clinically significant response rate higher than that for current standard treatments was observed in the DESTINY-Gastric02 and DESTINY-Gastric01 trials.

The side effects that were observed were in line with the known safety profile for Enhertu and are described in the Information for healthcare professionals. In view of the trial design, confirmatory efficacy re-

[3] In this context, "confirmed" means that there is stable tumour shrinkage that has been verified in at least 2 consecutive examinations.

[4] Objective response rate: the ORR is defined as the percentage of patients who respond to the treatment.

[5] 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.

[6] Duration of response (DOR) describes the period during which a patient responds to a treatment, i.e. the time during which tumour size is stably reduced or the tumour disappears altogether.

sults are required. The applicant has promised to submit data from the ongoing DESTINY-Gastric04 trial as evidence for the clinical benefits of Enhertu in this disease. On the basis of the above, Swissmedic has extended the indication for the medicinal product Enhertu, containing the active substance trastuzumab deruxtecan, in Switzerland. It is now also authorised for the second-line treatment of locally advanced or metastatic HER2-positive gastric or gastro-oesophageal junction adenocarcinoma in adults. This use has been temporarily authorised under Article 9a TPA, since not all clinical trials had been completed or were available at the time of authorisation. The temporary indication extension is contingent on the timely submission of the data requested by Swissmedic. Once these authorisation conditions have been met, the temporary authorisation can be converted into an authorisation without special conditions in the event of a positive benefit-risk assessment of the results.

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.