▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

NAME OF THE MEDICINAL PRODUCT.
Enhertu 100 mg powder for concentrate for solution for infusion.

QUALITATIVE AND QUANTITATIVE COMPOSITION.
One vial of powder for concentrate for solution for infusion contains 100 mg of trastuzumab deruxtecan. After reconstitution, one vial of 5 mL solution contains 20 mg/mL of trastuzumab deruxtecan. Trastuzumab deruxtecan is an antibody-drug conjugate (ADC) that contains a humanised anti-HER2 IgG1 monoclonal antibody (mAb) with the same amino acid sequence as trastuzumab, produced by mammalian (Chinese Hamster Ovary) cells, covalently linked to DXd, an exatecan derivative and a topoisomerase I inhibitor, via a tetrapeptide-based cleavable linker. Approximately 8 molecules of deruxtecan are attached to each antibody molecule.

PHARMACEUTICAL FORM.
Powder for concentrate for solution for infusion. White to yellowish-white lyophilised powder.

CLINICAL PARTICULARS.
Therapeutic indications
Breast cancer: *HER2-positive breast cancer:* Enhertu as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens. *HER2-low breast cancer:* Enhertu as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-low breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. Non-small cell lung cancer (NSCLC) Enhertu as monotherapy is indicated for the treatment of adult patients with advanced NSCLC whose tumours have an activating HER2 (ERBB2) mutation and who require systemic therapy following platinum-based chemotherapy with or without immunotherapy. Gastric cancer: Enhertu as monotherapy is indicated for the treatment of adult patients with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen.
Posology and method of administration
Enhertu should be prescribed by a physician and administered under the supervision of a healthcare professional experienced in the use of anticancer medicinal products. In order to prevent medicinal product errors, it is important to check the vial labels to ensure that the medicinal product being prepared and administered is Enhertu (trastuzumab deruxtecan) and not trastuzumab or trastuzumab emtansine. Enhertu should not be substituted with trastuzumab or trastuzumab emtansine. Patient selection: *HER2-positive breast cancer:* Patients treated with trastuzumab deruxtecan for breast cancer should have documented HER2-positive tumour status, defined as a score of 3 + by immunohistochemistry (IHC) or a ratio of ≥ 2.0 by *in situ* hybridization (ISH) or by fluorescence *in situ* hybridization (FISH) assessed by a CE-marked *in vitro* diagnostic (IVD) medical device. If a CE-marked IVD is not available, the HER2 status should be assessed by an alternate validated test. *HER2-low breast cancer:* Patients treated with trastuzumab deruxtecan should have documented HER2-low tumour status, defined as a score of IHC 1+ or IHC 2+/ISH-, as assessed by a CE-marked IVD medical device. If a CE-marked IVD is not available, the HER2 status should be assessed by an alternate validated test. *NSCLC* Patients treated with trastuzumab deruxtecan for advanced NSCLC should have an activating HER2 (ERBB2) mutation detected by a CE-marked *in vitro* diagnostic (IVD) medical device. If a CE-marked IVD is not available, the HER2 mutation status should be assessed by an alternate validated test. *Gastric cancer* Patients treated with trastuzumab deruxtecan for gastric or gastroesophageal junction cancer should have documented HER2-positive tumour status, defined as a score of 3 + by immunohistochemistry (IHC) or a ratio of ≥ 2 by *in situ* hybridization (ISH) or by fluorescence *in situ* hybridization (FISH), assessed by a CE-marked *in vitro* diagnostic (IVD) medical device. If a CE-marked IVD is not available, the HER2 status should be assessed by an alternate validated test. Posology. *Breast cancer:* The recommended dose of Enhertu is 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity. *NSCLC* The recommended dose of Enhertu is 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity. *Gastric cancer:* The recommended dose of Enhertu is 6.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity. The initial dose should be administered as a 90-minute intravenous infusion. If the prior infusion was well tolerated, subsequent doses of Enhertu may be administered as 30-minute infusions. The infusion rate of Enhertu should be slowed or interrupted if the patient develops infusion-related symptoms. Enhertu should be permanently discontinued in case of severe infusion reactions. Premedication. Enhertu is emetogenic, which includes delayed nausea and/or vomiting. Prior to each dose of Enhertu, patients should be premedicated with a combination regimen of two or three medicinal products (e.g., dexamethasone with either a 5-HT3 receptor antagonist and/or an NK1 receptor antagonist, as well as other medicinal products as indicated) for prevention of chemotherapy-induced nausea and vomiting. Dose modifications Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of Enhertu per guidelines listed below. Enhertu dose should not be re-escalated after a dose reduction is made.
Dose reduction schedule
Breast cancer and NSCLC: Recommended starting dose is 5.4 mg/kg. First dose reduction: 4.4 mg/kg. Second dose reduction: 3.2 mg/kg. Requirement for further dose reduction: discontinue treatment. *Gastric cancer:* Recommended starting dose is 6.4 mg/kg. First dose reduction: 5.4 mg/kg. Second dose reduction: 4.4 mg/kg. Requirement for further dose reduction: discontinue treatment.
Dose modifications for adverse reactions
Adverse reaction: ***Interstitial lung disease (ILD)/pneumonitis.*** Severity: Asymptomatic ILD/pneumonitis (Grade 1). Treatment modification: Interrupt Enhertu until resolved 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 • Consider corticosteroid treatment as soon as ILD/pneumonitis is suspected. Severity: Symptomatic ILD/pneumonitis (Grade 2 or greater). Treatment modification: • Permanently discontinue Enhertu • Promptly initiate corticosteroid treatment as soon as ILD/pneumonitis is suspected. Adverse reaction: ***Neutropenia.*** Severity: Grade 3 (less than 1.0-0.5 × 10^9/L). Treatment modification: • Interrupt Enhertu until resolved to Grade 2 or less, then maintain dose. Severity: Grade 4 (less than 0.5 × 10^9/L). Treatment modification: • Interrupt Enhertu until resolved to Grade 2 or less. • Reduce dose by one level. Adverse reaction: ***Febrile neutropenia.*** Severity: Absolute neutrophil count of less than 1.0 × 10^9/L and temperature greater than 38.3 °C or a sustained temperature of 38 °C or greater for more than one hour. Treatment modification: • Interrupt Enhertu until resolved. • Reduce dose by one level. Adverse reaction: ***Left ventricular ejection fraction (LVEF) decreased.*** Severity: LVEF greater than 45% and absolute decrease from baseline is 10% to 20%. Treatment modification: • Continue treatment with Enhertu. Severity: LVEF 40% to 45% and absolute decrease from baseline is less than 10%. Treatment modification: • Continue treatment with Enhertu. • Repeat LVEF assessment within 3 weeks. Severity: LVEF 40% to 45% and absolute decrease from baseline is 10% to 20%. Treatment modification: • Interrupt Enhertu. • 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. Severity: LVEF less than 40% or absolute decrease from baseline is greater than 20%. Treatment modification: • Interrupt Enhertu. • Repeat LVEF assessment within 3 weeks. • If LVEF of less than 40% or absolute decrease from baseline of greater than 20% is confirmed, permanently discontinue Enhertu. Severity: Symptomatic congestive heart failure (CHF). Treatment modification: • Permanently discontinue Enhertu. Toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v.5.0). Delayed or missed dose. If a planned dose is delayed or missed, it should be administered as soon as possible without waiting until the next planned cycle. The schedule of administration should be adjusted to maintain a 3-week interval between doses. The infusion should be administered at the dose and rate the patient tolerated in the most recent infusion. Special populations. *Elderly:* No dose adjustment of Enhertu is required in patients aged 65 years or older. Limited data are available in patients ≥ 75 years of age. *Renal impairment:* No dose adjustment is required in patients with mild (creatinine clearance [CLcr] ≥ 60 and < 90 mL/min) or moderate (CLcr ≥ 30 and < 60 mL/min) renal impairment. The potential need for dose adjustment in patients with severe renal impairment or end-stage renal disease cannot be determined as severe renal impairment was an exclusion criterion in clinical studies. A higher incidence of Grade 1 and 2 ILD/pneumonitis leading to an increase in discontinuation of therapy has been observed in patients with moderate renal impairment. In patients with moderate renal impairment at baseline who received Enhertu 6.4 mg/kg, a higher incidence of serious adverse reactions was observed compared to those with normal renal function. Patients with moderate or severe renal impairment should be monitored carefully for adverse reactions including ILD/pneumonitis. *Hepatic impairment:* No dose adjustment is required in patients with total bilirubin ≤ 1.5 times upper limit of normal (ULN), irrespective of aspartate transaminase (AST) value. The potential need for dose adjustment in patients with total bilirubin > 1.5 times ULN, irrespective of AST value, cannot be determined due to insufficient data; therefore, these patients should be monitored carefully. *Paediatric population:* The safety and efficacy of Enhertu in children and adolescents below the age of 18 years have not been established. No data are available. Method of administration. Enhertu is for intravenous use. It must be reconstituted and diluted by a healthcare professional and administered as an intravenous infusion. Enhertu must not be administered as an intravenous push or bolus.

CONTRAINDICATIONS
Hypersensitivity to the active substance or to any of the excipients: L-histidine, L-histidine hydrochloride monohydrate, Sucrose, Polysorbate 80.

UNDESIRABLE EFFECTS
Summary of the safety profile. *Enhertu 5.4 mg/kg.* The pooled safety population has been evaluated for patients who received at least one dose of Enhertu 5.4 mg/kg (n=1449) across multiple tumour types in clinical studies. The median duration of treatment in this pool was 9.8 months (range: 0.7 to 45.1 months). The most common adverse reactions were nausea (75.0%), fatigue (57.3%), vomiting (42.1%), alopecia (37.6%), neutropenia (35.2%), constipation (35.0%), anaemia (34.4%), decreased appetite (33.1%), diarrhoea (28.8%), transaminases increased (26.5%), musculoskeletal pain (26.2%), thrombocytopenia (24.5%) and leukopenia (23.7%). The most common National Cancer Institute – Common Terminology Criteria for Adverse Events (NCI-CTCAE v.5.0) Grade 3 or 4 adverse reactions were neutropenia (17.0%), anaemia (9.5%), fatigue (8.4%), leukopenia (6.4%), nausea (5.9%), thrombocytopenia (5.0%), lymphopenia (4.8%), hypokalaemia (3.8%), transaminases increased (3.6%), vomiting (2.7%), diarrhoea (2.0%), decreased appetite (1.7%), pneumonia (1.4%) and ejection fraction decreased (1.1%). Grade 5 adverse reactions occurred in 1.4% of patients, including ILD (1.0%). Dose interruptions due to adverse reactions occurred in 34.3% of patients treated with Enhertu. The most frequent adverse reactions associated with dose interruption were neutropenia (13.3%), fatigue (5.0%), anaemia (4.7%), leukopenia (3.7%), thrombocytopenia (3.0%), upper respiratory tract infection (2.7%) and ILD (2.6%). Dose reductions occurred in 20.6% of patients treated with Enhertu. The most frequent adverse reactions associated with dose reduction were fatigue (5.0%), nausea (4.9%), neutropenia (3.5%) and thrombocytopenia (2.1%). Discontinuation of therapy due to an adverse reaction occurred in 13.0% of patients treated with Enhertu. The most frequent adverse reaction associated with permanent discontinuation was ILD (9.2%). *Enhertu 6.4 mg/kg* The pooled safety population has been evaluated for patients who received at least one dose of Enhertu 6.4 mg/kg (n = 669), across multiple tumour types in clinical studies. The median duration of treatment in this pool was 5.7 months (range: 0.7 to 41.0 months). The most common adverse reactions were nausea (72.2%), fatigue (58.4%), decreased appetite (53.5%), anaemia (44.7%), neutropenia (43.5%), vomiting (40.1%), diarrhoea (35.9%), alopecia (35.4%), constipation (32.3%), thrombocytopenia (30.8%), leukopenia (29.3%) and transaminases increased (24.2%). The most common National Cancer Institute – Common Terminology Criteria for Adverse Events (NCI-CTCAE v.5.0) Grade 3 or 4 adverse reactions were neutropenia (28.7%), anaemia (22.6%), leukopenia (13.3%), thrombocytopenia (9.1%), fatigue (8.4%), decreased appetite (7.8%), lymphopenia (6.9%), nausea (5.8%), transaminases increased (4.3%), hypokalaemia (4.3%), pneumonia (3.1%), febrile neutropenia (2.8%), vomiting (2.4%), diarrhoea (2.2%), weight decreased (1.9%), blood alkaline phosphatase increased (1.6%), interstitial lung disease (ILD, 1.5%), dyspnoea (1.2%), ejection fraction decreased (1.2%), and blood bilirubine increased (1.2%). Grade 5 adverse reactions occurred in 2.7% of patients, including ILD (2.1%). Dose interruptions due to adverse reactions occurred in 40.7% of patients treated with Enhertu. The most frequent adverse reactions associated with dose interruption were neutropenia (16.6%), anaemia (7.8%), fatigue (5.7%), ILD (4.8%), leukopenia (4.2%), decreased appetite (3.7%), pneumonia (3.6%), upper respiratory tract infection (3.4%) and thrombocytopenia (3.1%). Dose reductions occurred in 31.1% of patients treated with Enhertu. The most frequent adverse reactions associated with dose reduction were fatigue (10.6%), neutropenia (6.6%), nausea (6.4%), decreased appetite (5.4%) and thrombocytopenia (3.0%). Discontinuation of therapy due to an adverse reaction occurred in 17.6% of patients treated with Enhertu. The most frequent adverse reaction associated with permanent discontinuation was ILD (12.9%). In patients with gastric cancer treated with Enhertu 6.4 mg/kg (n = 229), 25.3% received a transfusion within 28 days after onset of anaemia or thrombocytopenia. Transfusions were primarily for anaemia.
List of adverse reactions The adverse reactions in patients who received at least one dose of Enhertu in clinical studies are listed below. The adverse reactions are listed by MedDRA system organ class (SOC) and categories of frequency. Frequency categories are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness. **Adverse reactions in patients treated with trastuzumab deruxtecan 5.4 mg/kg and 6.4 mg/kg in multiple tumour types.** Infections and infestations: *Very common* (5.4 mg/kg and 6.4 mg/kg): Upper respiratory tract infection (includes for 5.4 mg/kg and 6.4 mg/kg influenza, influenza-like illness, nasopharyngitis, pharyngitis, rhinitis, laryngitis and upper respiratory tract infection); *Very Common* (6.4 mg/kg) and *Common* (5.4 mg/kg): Pneumonia. Blood and lymphatic system disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Anaemia (includes for 5.4 mg/kg and 6.4 mg/kg anaemia, haemoglobin decreased and red blood cell count decreased; includes for 5.4 mg/kg haematocrit decreased), Neutropenia (includes neutropenia and neutrophil count decreased), Thrombocytopenia (includes thrombocytopenia and platelet count decreased), Leukopenia (includes leukopenia and white blood cell count decreased), Lymphopenia (includes lymphopenia and lymphocyte count decreased; *Common* (6.4 mg/kg) and *Uncommon* (5.4 mg/kg): Febrile neutropenia. Metabolism and nutrition disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Hypokalaemia (includes hypokalaemia and blood potassium decreased), Decreased appetite; *Common* (5.4 mg/kg and 6.4 mg/kg): Dehydration. Nervous system disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Headache (includes for 5.4 mg/kg and 6.4 mg/kg headache and migraine; includes for 5.4 mg/kg sinus headache); *Very common* (6.4 mg/kg) and *Common* (5.4 mg/kg): Dysgeusia; *Very common* (5.4 mg/kg) and *Common* (6.4 mg/kg): Dizziness. Eye disorders: *Common* (5.4 mg/kg and 6.4 mg/kg): Dry eye, Vision blurred (includes vision blurred and visual impairment). Respiratory, thoracic and mediastinal disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Interstitial lung disease (For all tumour types at 5.4 mg/kg, interstitial lung disease includes events that were adjudicated as ILD: pneumonitis (n = 88), interstitial lung disease (n = 72), organising pneumonia (n = 6), pneumonia (n = 4), respiratory failure (n = 5), radiation pneumonitis (n = 2), alveolitis (n = 2), pulmonary toxicity (n = 2), pneumonia fungal (n = 1), pulmonary mass (n = 1), acute respiratory failure (n = 1), lung infiltration (n = 1), lymphangitis (n = 1), pulmonary fibrosis (n = 1), idiopathic interstitial pneumonia (n = 1), lung disorder (n = 1), hypersensitivity pneumonitis (n = 1) and lung opacity (n = 1). For all tumour types at 6.4 mg/kg, interstitial lung disease includes events that were adjudicated as ILD : pneumonitis (n = 75), interstitial lung disease (n = 39), organising pneumonia (n = 4), respiratory failure (n = 4), lung opacity (n = 2), pneumonia (n = 1) and radiation pneumonitis (n = 1)), dyspnoea, cough; *Very common* (5.4 mg/kg) and *Common* (6.4 mg/kg): Epistaxis. Gastrointestinal disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Nausea, Vomiting, Diarrhoea, Constipation, Abdominal pain (includes abdominal discomfort, gastrointestinal pain, abdominal pain, abdominal pain lower, and abdominal pain upper), Stomatitis (For all tumour types at 5.4 mg/kg and 6.4 mg/kg, includes stomatitis; For all tumour types at 5.4 mg/kg, includes aphthous ulcer, mouth ulceration, oral mucosa erosion and oral mucosal eruption); *Very common* (5.4 mg/kg) and *Common* (6.4 mg/kg): Dyspepsia; *Common* (5.4 mg/kg and 6.4 mg/kg): Abdominal distension, Gastritis, Flatulence. Hepatobiliary disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Transaminases increased (includes transaminases increased, alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, hepatic function abnormal, liver function test abnormal, liver function test increased and hypertransaminasaemia. Skin and subcutaneous tissue disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Alopecia; *Common* (5.4 mg/kg and 6.4 mg/kg): Rash (For all tumour types at 5.4 mg/kg and 6.4 mg/kg, includes rash, rash pustular, rash maculo-papular and rash pruritic. For all tumour types at 5.4 mg/kg, includes rash papular and rash macular), Pruritus, Skin hyperpigmentation (For all tumour types at 5.4 mg/kg and 6,4 mg/kg, includes skin hyperpigmentation and pigmentation disorder. For all tumour types at 5.4 mg/kg, includes skin discolouration). Musculoskeletal and connective tissue disorders: *Very common* (5.4 mg/kg and 6.4 mg/kg): Musculoskeletal pain (includes back pain, myalgia, pain in extremity, musculoskeletal pain, muscle spasms, bone pain, neck pain, musculoskeletal chest pain and limb discomfort). General disorders and administration site conditions: *Very common* (5.4 mg/kg and 6.4 mg/kg): Fatigue (includes asthenia, fatigue, malaise, and lethargy), Pyrexia; *Common* (5.4 mg/kg) and *Very common* (6.4 mg/kg): Oedema peripheral. Investigations: *Very common* (5.4 mg/kg and 6.4 mg/kg): Ejection fraction decreased (For all tumour types at 5.4 mg/kg, ejection fraction decreased includes laboratory parameters of LVEF decrease (n = 214) and/or preferred terms of ejection fraction decreased (n = 52), cardiac failure (n = 3), cardiac failure congestive (n = 1) and left ventricular dysfunction (n = 2). For all tumour types at 6.4 mg/kg, ejection fraction decreased includes laboratory parameters of LVEF decrease (n = 97) and/or preferred terms of ejection fraction decreased (n = 11) and left ventricular dysfunction (n = 1)), Weight decreased; *Common* (5.4 mg/kg and 6.4 mg/kg): Blood alkaline phosphatase increased, Blood bilirubin increased (For all tumour types at 5.4 mg/kg and 6.4 mg/kg, includes blood bilirubin increased, hyperbilirubinaemia and bilirubin conjugated increased; For all tumour types at 5.4 mg/kg, includes blood bilirubin unconjugated increased), Blood creatinine increased. Injury, poisoning and procedural complications: *Common* (5.4 mg/kg and 6.4 mg/kg): Infusion-related reactions (For all tumour types at 5.4 mg/kg, cases of infusion-related reactions include infusion-related reaction (n = 16) and hypersensitivity (n = 2). For all tumour types at 6.4 mg/kg, cases of infusion-related reactions include infusion-related reaction (n = 6) and hypersensitivity (n = 1). All cases of infusion-related reactions were Grade 1 and Grade 2). Description of selected adverse reactions *Interstitial lung disease/pneumonitis* In patients treated with Enhertu 5.4 mg/kg in clinical studies across multiple tumour types (n = 1449), ILD occurred in 12.5% of patients. Most ILD cases were Grade 1 (3.2%) and Grade 2 (7.4%). Grade 3 cases occurred in 0.8% and no Grade 4 cases occurred. Grade 5 (fatal) events occurred in 1.0% of patients. Median time to first onset was 5.5 months (range: 26 days to 31.5 months). In patients treated with Enhertu 6.4 mg/kg in clinical studies across multiple tumour types (n = 669), ILD occurred in 17.9% of patients. Most ILD cases were Grade 1 (4.9%) and Grade 2 (9.4%). Grade 3 cases occurred in 1.3% and Grade 4 cases occurred in 0.1% of patients. Grade 5 (fatal) events occurred in 2.1% of patients. One patient had pre-existing ILD that worsened post treatment leading to Grade 5 (fatal) ILD. Median time to first onset was 4.2 months (range: -0.5 to 21.0). *Neutropenia* In patients treated with Enhertu 5.4 mg/kg in clinical studies (n = 1449) across multiple tumour types, neutropenia was reported in 35.2% of patients and 17.0% had Grade 3 or 4 events. Median time of onset was 43 days (range: 1 day to 31.9 months), and median duration of the first event was 22 days (range: 1 day to 17.1 months). Febrile neutropenia was reported in 0.9% of patients and 0.1% were Grade 5. In patients treated with Enhertu 6.4 mg/kg in clinical studies across multiple tumour types (n = 669), neutropenia was reported in 43.5% of patients and 28.7% had Grade 3 or 4 events. Median time of onset was 16 days (range: 1 day to 24.8 months), and median duration of the first event was 9 days (range: 2 days to 17.2 months). Febrile neutropenia was reported in 3.0% of patients and 0.1% were Grade 5. *Left ventricular ejection fraction decrease* In patients treated with Enhertu 5.4 mg/kg in clinical studies across multiple tumour types (n = 1449), LVEF decrease was reported in 57 patients (3.9%), of which 10 (0.7%) were Grade 1, 40 (2.8%) were Grade 2 and 7 (0.5%) were Grade 3. The observed frequency of LVEF decreased based on laboratory parameters (echocardiogram or MUGA scanning) was 202/1341 (15.1%) for Grade 2 and 12/1341 (0.9%) for Grade 3. Treatment with Enhertu has not been studied in patients with LVEF less than 50% prior to initiation of treatment. In patients treated with Enhertu 6.4 mg/kg in clinical studies across multiple tumour types (n = 669), LVEF decrease was reported in 12 patients (1.8%), of which 1 (0.1%) was Grade 1, 8 (1.2%) were Grade 2, and 3 (0.4%) were Grade 3. The observed frequency of LVEF decreased based on laboratory parameters (echocardiogram or MUGA scanning) was 89/597 (14.9%) for Grade 2, and 8/597 (1.3%) for Grade 3. Infusion-related reactions In patients treated with Enhertu 5.4 mg/kg in clinical studies (n = 1449) across multiple tumour types, infusion-related reactions were reported in 18 patients (1.2%), all of which were Grade 1 or Grade 2 severity. No Grade 3 events were reported. Three events (0.2%) of infusion-related reactions led to dose interruptions, and no events led to discontinuation. In patients treated with Enhertu 6.4 mg/kg in clinical studies (n = 669) across multiple tumour types, infusion-related reactions were reported in 7 patients (1.0%), all of which were Grade 1 or Grade 2 severity. No Grade 3 events were reported. One event (0.1%) of infusion-related reaction led to dose interruption, and no events led to discontinuation. Immunogenicity As with all therapeutic proteins, there is a potential for immunogenicity. Across all doses evaluated in clinical studies, 2.1% (47/2213) of evaluable patients developed antibodies against trastuzumab deruxtecan following treatment with Enhertu. The incidence of treatment-emergent neutralising antibodies against trastuzumab deruxtecan was 0.1% (2/2213). There was no association between development of antibodies and allergic-type reactions. Paediatric population Safety has not been established in this population. Elderly In patients treated with Enhertu 5.4 mg/kg in clinical studies across multiple tumour types (n = 1449), 24.2% were 65 years or older and 4.3% were 75 years or older. There was a higher incidence of Grade 3-4 adverse reactions observed in patients aged 65 years or older (50.0%) as compared to patients younger than 65 years old (42.7%), leading to more discontinuations due to adverse reactions. Of the 669 patients across multiple tumour types in clinical studies treated with Enhertu 6.4 mg/kg, 39.2% were 65 years or older and 7.6% were 75 years or older. The incidence of Grade 3-4 adverse reactions observed in patients 65 years or older was 59.9% and 62.9% in younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients 75 years of age or older (64.7%) compared to patients less than 75 years of age (61.5%). In patients 75 years or older, there was a higher incidence of serious adverse reactions (37.3%) and fatal events (7.8%) compared to patients less than 75 years (20.7% and 2.3%). Data are limited to establish the safety in patients 75 years or older. Ethnic differences In clinical studies, no relevant differences in exposure or efficacy were observed between patients of different ethnic groups. Asian patients receiving Enhertu 6.4 mg/kg had a higher incidence (≥10% difference) of neutropenia (58.1% vs. 18.6%), anaemia (51.1% vs. 32.4%), leukopenia (42.7% vs. 6.9%), thrombocytopenia (40.5% vs. 15.4%), and lymphopenia (17.6% vs. 7.3%) compared to non-Asian patients. In Asian patients, 4.3% experienced a bleeding event within 14 days after onset of thrombocytopenia compared to 1.6% of non-Asian patients.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via: **Belgium:** Federal Agency for Medicines and Health Products – FAMHP, Avenue Galilée 5/03, 1210 BRUSSELS or PO Box 97, 1000 BRUSSELS, Madou. Website: https://www.famhp.be/en/side_effect. e-mail: adr@fagg.be. **Luxembourg:** Centre Régional de Pharmacovigilance de Nancy or Division de la pharmacie des médicaments de la Direction de la santé. Site internet : www.guichet.lu/pharmacovigilance

Ex-factory price excl. VAT		Reimbursed
100 mg	€ 1.600,00	100%

DELIVERY MODE. On medical prescription.

MARKETING AUTHORISATION HOLDER: Daiichi Sankyo Europe GmbH, Zielstattstrasse 48, 81379 Munich, Germany.

MARKETING AUTHORISATION NUMBER(S): EU/1/20/1508/001.

DATE OF REVISION OF THE TEXT: 10/2023.
Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.