EMA/556006/2024

European Medicines Agency decision

P/0397/2024

of 5 December 2024

on the agreement of a paediatric investigation plan and on the granting of a deferral for trastuzumab deruxtecan (Enhertu), (EMEA-002978-PIP02-24) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Daiichi Sankyo Europe GmbH on 26 February 2024 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 November 2024, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for trastuzumab deruxtecan (Enhertu), powder for concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for trastuzumab deruxtecan (Enhertu), powder for concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Daiichi Sankyo Europe GmbH, Zielstattstr. 48, 81379 – Munich, Germany.

EMA/PDCO/393179/2024
Amsterdam, 15 November 2024

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral

EMEA-002978-PIP02-24

Scope of the application

Active substance(s):

Trastuzumab deruxtecan

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of all conditions in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Pharmaceutical form(s):

Powder for concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Daiichi Sankyo Europe GmbH

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Daiichi Sankyo Europe GmbH submitted for agreement to the European Medicines Agency on 26 February 2024 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 2 April 2024.

Supplementary information was provided by the applicant on 9 August 2024. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of all conditions in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

2.1.1. Indication(s) targeted by the PIP

Treatment of unresectable or metastatic HER2-expressing solid tumours

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate dosage form.
Non-clinical studies	**Study 2 (Tumour microarray study)** Study to determine the prevalence of human epidermal growth factor receptor 2 (HER2) in human paediatric tumours **Study 3 (Study 1034)** Study to determine in vitro and in vivo antitumour activity of trastuzumab deruxtecan (T-DXd) in Wilms tumour and malignant rhabdoid tumours. **Study 4 (Study 1057)** Study to determine HER2 expression and in vitro antitumour activity of T-DXd/DXd and in vivo antitumour activity of T-DXd in human paediatric central nervous system tumours.
Clinical studies	**Study 5** Open-label, single arm, two part, dose-finding (Part 1) and expansion (Part 2) trial to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety (Part 1) in children from 2 years to less than 12 years of age, and activity (Part 2) of trastuzumab deruxtecan (T-DXd) in children from 2 years to less than 18 years of

	age (and adults) with relapsed/refractory desmoplastic small round cell tumour (DSRCT), relapsed/refractory Wilms tumour and other relevant solid tumour types based on results from PIP studies 2 and 4. **Study 6** Randomised, open-label study to evaluate the efficacy, safety, and pharmacokinetics of T-DXd plus/minus comparator (to be determined) versus comparator (to be determined) in children with unresectable or metastatic HER2-expressing paediatric tumours (based on results from PIP study 5).
Modelling and simulation analyses	**Study 7** Modelling and simulation analyses, to evaluate the use of T-DXd for treatment of unresectable or metastatic HER2-expressing solid tumours from birth to less than 18 years of age with unresectable or metastatic HER2-expressing solid tumours.
Other studies	Not applicable
Extrapolation plan	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By June 2032
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of breast malignant neoplasms

Authorised 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 (see section 4.2)

  - Invented name: Enhertu
  - Authorised pharmaceutical form: powder for concentrate for solution for infusion
  - Authorised route of administration: For intravenous use after reconstitution and dilution
  - Authorised via centralised procedure

2. Treatment of Lung Cancer

Authorised indication:

- 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

  - Invented name: Enhertu
  - Authorised pharmaceutical form: powder for concentrate for solution for infusion
  - Authorised route of administration: For intravenous use after reconstitution and dilution
  - Authorised via centralised procedure

3. Treatment of intestinal malignant neoplasms

Authorised indication:

- 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

  - Invented name: Enhertu
  - Authorised pharmaceutical form: powder for concentrate for solution for infusion
  - Authorised route of administration: For intravenous use after reconstitution and dilution
  - Authorised via centralised procedure