MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-101404-PIP01-24) and to the deferral

MHRA-101404-PIP01-24-M01

Scope of the Application

Active Substance(s)

TRASTUZUMAB DERUXTECAN

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 UK LIMITED

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, DAIICHI SANKYO UK LIMITED submitted to the licensing authority on 16/04/2025 10:09 BST an application for a Modification

The procedure started on 06/05/2025 09:34 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

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

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-101404-PIP01-24-M01

Of 25/07/2025 16:27 BST

On the adopted decision for TRASTUZUMAB DERUXTECAN (MHRA-101404-PIP01-24-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for TRASTUZUMAB DERUXTECAN, Powder for concentrate for solution for infusion , INTRAVENOUS USE .

This decision is addressed to DAIICHI SANKYO UK LIMITED, Building 4, Uxbridge Business Park, Sanderson Road , Uxbridge, UNITED KINGDOM, UB8 1DH

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

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

2.2 Indication(s) targeted by the PIP:

Treatment of unresectable or metastatic HER2-expressing solid tumours

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Powder for concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age appropriate dosage form and/or strength.
Non-Clinical Studies	3	Study 2 Study to determine the prevalence of human epidermal growth factor receptor 2 (HER2) in human paediatric tumours. Study 3 Deleted during procedure MHRA-101404-PIP01-24-M01. Study 4 (1034) Study to determine in vitro and in vivo antitumour activity of T-DXd in Wilms tumour and malignant rhabdoid tumours. Study 5 (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	2	Study 6 Open-label, single arm, two part trial to identify a recommended phase 2 dose (RP2D), and evaluate pharmacokinetics (PK), pharmacodynamics (PD) and safety (part one) and activity (part two) 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 5. Study 7 Randomised, open-

		label trial to evaluate the safety, efficacy and pharmacokinetics of T-DXd against an appropriate comparator in a selected paediatric population to be further defined based on results from study 6.
Extrapolation, Modeling & Simulation Studies	1	Study 8 Modelling and simulation analysis to evaluate the use and determine the dose of trastuzumab deruxtecan (T-DXd) in the proposed paediatric indication in children less than 18 years of age.
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/06/2032
Deferral of one or more studies contained in the paediatric investigation plan:	Yes