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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and refuse a waiver

MHRA-100466-PIP01-22

Scope of the Application

Active Substance(s)

zilovertamab vedotin

Condition(s)

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

Pharmaceutical Form(s)

Powder for concentrate for solution for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Merck Sharp & Dohme (UK) Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Merck Sharp & Dohme (UK) Limited submitted to the licensing authority on 06/10/2022 11:32 BST an application for a Paediatric Investigation Plan

The procedure started on 09/03/2023 09:02 GMT

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 agree a paediatric investigation plan and grant a deferral and refuse a waiver

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-100466-PIP01-22

Of 24/03/2023 14:54 GMT

On the adopted decision for zilovertamab vedotin (MHRA-100466-PIP01-22) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for zilovertamab vedotin, Powder for concentrate for solution for infusion , INTRAVENOUS USE .

This decision is addressed to Merck Sharp & Dohme (UK) Limited, 120 Moorgate, London, UNITED KINGDOM, EC2M 6UR

ANNEX I

1. Waiver

1.1 Condition:

Condition1: Treatment of malignant neoplasms of haematopoietic and lymphoid tissue The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Powder for concentrate for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: Not Applicable Reason for Refusing Waiver: From birth to less than 6 months of age: the MHRA disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe. From 6 months to less than 1 year of age: the disease or condition for which the specific medicinal product is intended, does occur in the paediatric population(s). The waiver request is therefore refused by the MHRA Condition 2: Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic, and lymphoid tissue) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Powder for concentrate for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: Not Applicable Reason for Refusing Waiver: the MHRA disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe The waiver request is therefore refused by the MHRA

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of malignant neoplasms of haematopoietic and lymphoid tissue Condition 2: Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic, and lymphoid tissue)

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of patients with a relapsed or refractory solid or haematological malignancy identified based on the results of PIP study 1 as monotherapy or in combination with standard of care. Condition 2: Treatment of patients with a relapsed or refractory solid or haematological malignancy identified based on the results of PIP study 1 as monotherapy or in combination with standard of care.

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

For both conditions: The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both conditions: Powder for concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	(Same studies for both Conditions) Study 1 (MK-2140 Paediatric Study) Open label, two part trial to evaluate the recommended phase 2 dose, pharmacokinetics (PK), pharmacodynamics (PD), safety (part 1), and safety, activity and immunogenicity (Part 2) of zilovertamab vedotin in children from birth to less than 18 years of age with relapsed or refractory solid tumours or haematological or lymphoid malignancies for which all treatment options are exhausted (Part 1) and with relapsed or refractory B-

		Acute lymphoblastic leukaemia (B-ALL), diffuse large B cell lymphoma (DLBCL)/Burkitt lymphoma, Ewing sarcoma, or neuroblastoma (Part 2). Study 2 Randomised, controlled trial to evaluate safety, efficacy, immunogenicity of zilovertamab vedotin monotherapy or in combination with standard of care compared to standard of care in children from birth to less than 18 years of age with a malignancy identified based on data from Study 1.
Extrapolation, Modeling & Simulation Studies	1	(Same study for both Conditions) Study 3 Modelling and simulation study, to support dose finding of zliovertamab vedotin in children from birth to less than 18 years of age with relapsed or refractory solid tumours or haematological malignancies.
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:	31/12/2035
Deferral of one or more studies contained in the paediatric investigation plan:	Yes