EMA/146751/2023

European Medicines Agency decision

P/0130/2023

of 13 April 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver for zilovertamab vedotin (EMEA-003257-PIP01-22) 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 Merck Sharp & Dohme (Europe) Inc. on 27 May 2022 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 February 2023, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 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 and on the refusal of a waiver.

(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.

(4) It is therefore appropriate to adopt a decision refusing a waiver.

[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 zilovertamab vedotin, powder 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 zilovertamab vedotin, powder 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

A waiver for zilovertamab vedotin, powder 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 refused.

Article 4

This decision is addressed to Merck Sharp & Dohme (Europe) Inc., Lynxbinnenhof 5,1200 - Brussels, Belgium.

EMA/926799/2022
Amsterdam, 24 February 2023

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

EMEA-003257-PIP01-22

Scope of the application

Active substance(s):

Zilovertamab vedotin

Invented name and authorisation status:

See Annex II

Condition(s):

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

Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Merck Sharp & Dohme (Europe) Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe) Inc. submitted for agreement to the European Medicines Agency on 27 May 2022 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 11 July 2022.

Supplementary information was provided by the applicant on 21 November 2022. 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;
   - to refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population and the above mentioned condition(s) as it does not meet the grounds detailed in Article 11(1) 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 and the subset(s) of the paediatric population and condition(s) covered by the waiver 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

1.1. Condition:

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

The request for the waiver applied to:

- the paediatric population from birth to less than 6 months of age;
- powder for solution for infusion, intravenous use;

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;

Because:

- the PDCO 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 PDCO.

1.2. Condition:

Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

The request for the waiver applied to:

- the paediatric population from birth to less than 6 months of age;
- powder for solution for infusion, intravenous use;

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;

Because:

- the PDCO 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 PDCO.

2. Paediatric investigation plan

2.1. Condition:

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

2.1.1. Indication(s) targeted by the PIP

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

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 solution for infusion

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**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 (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.
Modelling and simulation studies	**Study 3** Modelling and simulation study, to support dose finding 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.
Other studies	Not applicable
Extrapolation plan	Not applicable

2.2. Condition:

Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

2.2.1. Indication(s) targeted by the PIP

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

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Powder for solution for infusion

2.2.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1** (MK-2140 Paediatric Study) Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic, and lymphoid tissue) **Study 2** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic, and lymphoid tissue)
Modelling and simulation studies	**Study 3** Same as for the condition treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic, and lymphoid tissue)
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:	Yes
Date of completion of the paediatric investigation plan:	By December 2035
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:

The product is not authorised anywhere in the European Community.