EMA/374089/2024

European Medicines Agency decision

P/0312/2024

of 22 August 2024

on the acceptance of a modification of an agreed paediatric investigation plan for avelumab (Bavencio), (EMEA-001849-PIP02-15-M05) 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 European Medicines Agency's decision P/0071/2017 issued on 17 March 2017, the decision P/0361/2017 issued on 1 December 2017, the decision P/0242/2018 issued on 15 August 2018, the decision P/0504/2020 issued on 22 December 2020, and the decision P/0546/2021 issued on 31 December 2021,

Having regard to the application submitted by Merck Healthcare KGaA on 23 April 2024 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 July 2024, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the 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

Changes to the agreed paediatric investigation plan for avelumab (Bavencio), concentrate for solution for infusion, intravenous use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Merck Healthcare KGaA, Frankfurter Strasse 250, 64293 – Darmstadt, Germany.

EMA/PDCO/227009/2024
Amsterdam, 26 July 2024

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001849-PIP02-15-M05

Scope of the application

Active substance(s):

Avelumab

Invented name and authorisation status:

See Annex II

Condition(s):

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

Treatment of malignant neoplasms of lymphoid tissue

Treatment of malignant neoplasms of the central nervous system

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Merck Healthcare KGaA

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck Healthcare KGaA submitted to the European Medicines Agency on 23 April 2024 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0071/2017 issued on 17 March 2017, the decision P/0361/2017 issued on 1 December 2017, the decision P/0242/2018 issued on 15 August 2018, the decision P/0504/2020 issued on 22 December 2020, and the decision P/0546/2021 issued on 31 December 2021.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 27 May 2024.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

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

The measures and timelines of the 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)

Waiver

1.1. Condition

Treatment of malignant neoplasms of lymphoid tissue

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- concentrate for solution for infusion, intravenous use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

1.2. Condition

Treatment of malignant neoplasms of the central nervous system

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- concentrate for solution for infusion, intravenous use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition

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

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth to less than 18 years old with a relapsed or refractory solid tumour or with a solid tumour as part of the first line treatment

2.1.2.

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

From birth to less than 18 years of age

2.1.4. Pharmaceutical form(s)

Concentrate for solution for infusion

2.1.5. Measures

Area	Description
Quality-related studies	Not applicable.
Non-clinical studies	**Study 1** Exploratory toxicity/efficacy non-clinical study in a syngeneic mouse model **Study 2** Collection and analysis of data from literature and databases of paediatric tumour samples relative to tumour genetic mutations and tumour gene and neoantigens expression **Study 3** Non-clinical biomarker study in paediatric tumour tissues
Clinical studies	**Study 4** Open-label study to evaluate pharmacokinetics, pharmacodynamics, safety and anti-cancer activity of avelumab in paediatric patients from birth to less than 18 years of age with a refractory or relapsed solid tumour, including lymphomas and tumours of the central nervous system, or for which no effective treatment is known **Study 5** deleted in procedure EMEA-001849-PIP02-15-M03
Extrapolation, modelling and simulation studies	**Study 6** Adult population pharmacokinetic PK (POPPK) model study
Other studies	Not applicable.
Other measures	Not applicable.

2.2. Condition

Treatment of malignant neoplasms of the central nervous system

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from 2 years to less than 18 years old with a refractory or relapsed tumour of the central nervous system or with a tumour of the central nervous system as part of first line treatment

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

From 2 years to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.2.4. Measures

Area	Description
Quality-related studies	Not applicable.
Non-clinical studies	**Study 1** same as for condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms). **Study 2** same as for condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms). **Study 3** same as for condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms).
Clinical studies	**Study 4** same as for condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms). **Study 5** deleted in procedure EMEA-001849-PIP02-15-M05 **Study 7** added in procedure EMEA-001849-PIP02-15-M03 Open-label, single-arm study to evaluate pharmacokinetics, safety and tolerability (dose-escalation part) of avelumab used in combination with lenvatinib in paediatric patients from 2 years to less than 18 years of age with a primary central nervous system malignancy that has progressed after at least one prior therapy. Expansion part of the study deleted in procedure EMEA-001849-PIP02-15-M05
Extrapolation, modelling and simulation studies	**Study 6** same as for condition treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms).
Other studies	Not applicable.
Other measures	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 September 2025
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):

Treatment of Merkel cell carcinoma

Authorised indication(s):

- Bavencio is indicated as monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (MCC).
- Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms)

Authorised indication(s):

- Bavencio in combination with axitinib is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC).
- Bavencio is indicated as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who are progression-free following platinum-based chemotherapy

Authorised pharmaceutical form(s): concentrate for solution for infusion

Authorised route(s) of administration: intravenous use

Authorised via centralised procedure