EMA/709765/2017

European Medicines Agency decision

P/0361/2017

of 1 December 2017

on the acceptance of a modification of an agreed paediatric investigation plan for avelumab (Bavencio) (EMEA-001849-PIP02-15-M01) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

European Medicines Agency decision

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on the acceptance of a modification of an agreed paediatric investigation plan for avelumab (Bavencio) (EMEA-001849-PIP02-15-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary 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,

Having regard to the application submitted by Merck KGaA on 24 July 2017 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 October 2017, 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.

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for avelumab (Bavencio), concentrate for solution for infusion, intravenous use, 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 KGaA, Frankfurter Strasse 250, 64293 – Darmstadt, Germany.

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

EMA/PDCO/475275/2017
London, 13 October 2017

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

EMEA-001849-PIP02-15-M01

Scope of the application

Active substance(s):

Avelumab

Invented name:

Bavencio

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

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Merck KGaA

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck KGaA submitted to the European Medicines Agency on 24 July 2017 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0071/2017 issued on 17 March 2017.

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

The procedure started on 15 August 2017.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. Amendment of the scope of the Paediatric Investigation Plan to include other conditions.

Opinion

1. 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 in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the 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 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. 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)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	3	**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	2	**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 (phase I), and to evaluate safety and efficacy in at least two expansion cohorts in selected tumour types (phase II). **Study 5** Randomized, active-controlled study to evaluate efficacy and safety of avelumab in combination with standard of care in children from birth to less than 18 years of age with a paediatric solid tumour selected on the basis of the results of Study 1, Study 2, Study 3 and Study 4.
Extrapolation, modelling and simulation studies	1	**Study 6** Adult population pharmacokinetic PK (POPPK) model study
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition

Treatment of malignant neoplasms of lymphoid tissue

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth to less than 18 years old with a refractory or relapsed Hodgkin or non-Hodgkin lymphoma, or with Hodgkin or non-Hodgkin lymphoma as part of first line treatment.

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)

Concentrate for solution for infusion

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.

Non-clinical studies	3	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	2	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 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)
Extrapolation, modelling and simulation studies	1	Study 5 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	0	Not applicable.
Other measures	0	Not applicable.

2.3. Condition

Treatment of malignant neoplasms of the central nervous system

2.3.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth 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.

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

From birth to less than 18 years of age

2.3.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.3.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	3	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	2	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 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)
Extrapolation, modelling and simulation studies	1	Study 5 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	0	Not applicable.
Other measures	0	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 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of Merkel cell carcinoma

Authorised indication(s):

Bavencio is indicated as monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use