EMA/8040/2017

European Medicines Agency decision

P/0004/2017

of 13 January 2017

on the acceptance of a modification of an agreed paediatric investigation plan for nivolumab (Opdivo), (EMEA-001407-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.

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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 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/0040/2016 issued on 19 February 2016,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 26 September 2016 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 16 December 2016, 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.

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for nivolumab (Opdivo), 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0064/2014 issued on 7 March 2014, including subsequent modifications thereof.

Article 3

This decision is addressed to Bristol-Myers Squibb Pharma EEIG, Uxbridge Business Park, Sanderson Road, UB8 1DH – Uxbridge, United Kingdom.

EMA/PDCO/641376/2016
London, 16 December 2016

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

EMEA-001407-PIP02-15-M01

Scope of the application

Active substance(s):

Nivolumab

Invented name:

Opdivo

Condition(s):

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:

Bristol-Myers Squibb Pharma EEIG

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb Pharma EEIG submitted to the European Medicines Agency on 26 September 2016 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/0040/2016 issued on 19 February 2016.

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

The procedure started on 18 October 2016.

Scope of the modification

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

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 Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. 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)

1. Waiver

1.1. Condition:

Treatment of malignant neoplasms of lymphoid tissue

The waiver applies to:

- the paediatric population from birth to less than 6 months;
- concentrate for solution for infusion;
- 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 6 months;
- concentrate for solution for infusion;
- 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 malignant neoplasms of lymphoid tissue

2.1.1. Indication(s) targeted by the PIP

- Treatment of paediatric patients with a relapsed or refractory Hodgkin lymphoma in the age group from 5 years to less than 18 years.
- Treatment of paediatric patients with a relapsed or refractory non-Hodgkin lymphoma in the age group from 6 months to less than 18 years old.

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

From 6 months 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	0	Not applicable.
Clinical studies	3	**Study 1** Open-label, multi-centre trial to evaluate pharmacokinetics, pharmacodynamics, toxicity, safety and anti-cancer activity of nivolumab and of nivolumab in combination with ipilimumab in paediatric patients from 1 year to less than 18 years of age with a PD-L1 positive refractory or relapsed malignant solid tumour, with an expansion phase evaluating nivolumab in paediatric patients from 1 year to less than 18 years of age (and adults) with a PD-L1 positive refractory or relapsed Ewing sarcoma, osteosarcoma, rhabdomyosarcoma or neuroblastoma, for which no effective treatment is known (same as study 2 in EMEA-001407-PIP01-12). **Study 3** Randomised, controlled trial to evaluate pharmacokinetics, efficacy and safety of nivolumab in combination with a rationally selected other medicine compared to standard anti-cancer care in patients from birth to less than 18 years of age with a paediatric solid malignant tumour type or in patients from 6 months to less than 18 years of age with a malignant neoplasm of lymphoid tissue, determined based on results of study 1 (same as study 3 in EMEA-001407-PIP01-12) **Study 4** Open label, single arm trial to assess the safety and activity of nivolumab combined with brentuximab vedotin in paediatric patients from 5 to less than 18 years (and adults) with a relapsed or refractory Hodgkin lymphoma followed by brentuximab vedotin in combination with bendamustine in case of suboptimal response
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	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 6 months to less than 18 years of age with a recurrent or progressive high-grade glioma

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

From 6 months 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	0	Not applicable.
Clinical studies	2	**Study 1** Same as for condition treatment of malignant neoplasms of lymphoid tissue **Study 2** Multi-centre, open-label, single-arm trial of nivolumab to evaluate safety, pharmacodynamics and anti-tumour activity in patients from 6 months to less than 18 years of age with a recurrent or refractory central nervous system tumour
Extrapolation, modelling and simulation studies	0	Not applicable.
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 August 2024
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 melanoma

Authorised indication(s):

- Opdivo as monotherapy or in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.

2. Treatment of non-small cell lung cancer

Authorised indication(s):

- Opdivo is indicated for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy in adults.

3. Treatment of renal cell carcinoma

Authorised indication(s):

- Opdivo as monotherapy is indicated for the treatment of advanced renal cell carcinoma after prior therapy in adults.

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use