EMA/101776/2018

European Medicines Agency decision

P/0049/2018

of 22 February 2018

on the acceptance of a modification of an agreed paediatric investigation plan for nivolumab (Opdivo), (EMEA-001407-PIP01-12-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

P/0049/2018

of 22 February 2018

on the acceptance of a modification of an agreed paediatric investigation plan for nivolumab (Opdivo), (EMEA-001407-PIP01-12-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/0064/2014 issued on 7 March 2014.

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 6 November 2017 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 January 2018, 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 is addressed to Bristol-Myers Squibb Pharma EEIG, Uxbridge Business Park, Sanderson Road, UB8 1DH – Uxbridge, United Kingdom.

EMA/PDCO/781711/2017
London, 26 January 2018

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

EMEA-001407-PIP01-12-M01

Scope of the application

Active substance(s):

Nivolumab

Invented name:

Opdivo

Condition(s):

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

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

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, Bristol-Myers Squibb Pharma EEIG submitted to the European Medicines Agency on 6 November 2017 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/0064/2014 issued on 7 March 2014.

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

The procedure started on 28 November 2017.

Scope of the modification

Some measures 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 Norwegian Paediatric Committee member agrees 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 all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)

The waiver applies to:

- The paediatric population from birth to less than 6 months of age;
- concentrate for solution for infusion, for 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 nervous system, haematopoietic and lymphoid tissue)

2.1.1. Indication(s) targeted by the PIP

- Treatment of a paediatric malignant solid tumour in paediatric patients from 6 months to less than 18 years old
- Treatment of patients with unresectable or metastatic melanoma in the age group from 12 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 studies**	**Description**
Quality-related studies	0	Not applicable
Non-clinical studies	1	**Study 1** Non-clinical biomarker study in paediatric tumour tissue

Clinical studies	2	**Study 2** 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 refractory or relapsed malignant solid tumour for which no effective treatment is known, with an expansion phase evaluating nivolumab in paediatric patients from 1 year to less than 18 years of age (and adults) with a refractory or relapsed malignant solid tumour such as Ewing sarcoma, osteosarcoma, rhabdomyosarcoma and neuroblastoma, for which no effective treatment is known **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 determined based on results of studies 1 and 2
Extrapolation, modelling & simulation studies	1	**Study 4** Study to generate paediatric dosing recommendations for nivolumab alone and in combination with ipilimumab
Other studies	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety 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 all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)

Authorised indication(s):

- OPDIVO as monotherapy or in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.
- OPDIVO is indicated for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy in adults.
- OPDIVO as monotherapy is indicated for the treatment of advanced renal cell carcinoma after prior therapy in adults.
- OPDIVO as monotherapy is indicated for the treatment of squamous cell cancer of the head and neck in adults progressing on or after platinum-based therapy.
- OPDIVO as monotherapy is indicated for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy.

2. Treatment of malignant neoplasms of lymphoid tissue

Authorised indication(s):

- OPDIVO as monotherapy is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin.

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use