EMA/318795/2021

European Medicines Agency decision

P/0237/2021

of 14 June 2021

on the acceptance of a modification of an agreed paediatric investigation plan for nivolumab (Opdivo), (EMEA-001407-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 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, the decision P/0004/2017 issued on 13 January 2017, the decision P/0050/2018 issued on 22 February 2018, the decision P/0027/2020 issued on 9 January 2020 and the decision P/0433/2020 issued on 5 November 2020,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 12 February 2021 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 21 May 2021, 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, Plaza 254, Blanchardstown Corporate Park 2, D15 T867 - Dublin 15, Ireland.

EMA/PDCO/142790/2021
Amsterdam, 21 May 2021

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

EMEA-001407-PIP02-15-M05

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

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 12 February 2021 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 decision P/0004/2017 issued on 13 January 2017, the decision P/0050/2018 issued on 22 February 2018, the decision P/0027/2020 issued on 9 January 2020 and the decision P/0433/2020 issued on 5 November 2020.

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

The procedure started on 23 March 2021.

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

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; 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).

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; 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

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 of age

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 of age

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	2	**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 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 refractory or relapsed Ewing sarcoma, osteosarcoma, rhabdomyosarcoma or neuroblastoma, for which no effective treatment is known (CA209070, same as study 2 in EMEA-001407-PIP01-12) **Study 3** deleted in procedure EMEA-001407-PIP02-15-M04 **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 (CA209744)
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	0	Not applicable
Other measures	0	Not applicable

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 (and adults) with a recurrent or refractory central nervous system tumour (CA209908)
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 May 2024

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. Relative to nivolumab monotherapy, an increase in progression-free survival (PFS) and overall survival (OS) for the combination of nivolumab with ipilimumab is established only in patients with low tumour PD-L1 expression

- OPDIVO as monotherapy is indicated for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

- OPDIVO in combination with ipilimumab and 2 cycles of platinum-based chemotherapy is indicated for the first-line treatment of metastatic non-small cell lung cancer in adults whose tumours have no sensitising EGFR mutation or ALK translocation.

- OPDIVO as monotherapy is indicated for the treatment of locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults.

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

- OPDIVO in combination with ipilimumab is indicated for the first-line treatment of adult patients with intermediate/poor-risk advanced renal cell carcinoma.

- OPDIVO in combination with cabozantinib is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma.

- OPDIVO as monotherapy is indicated for the treatment of recurrent or metastatic 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.

- OPDIVO as monotherapy is indicated for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platium-based combination chemotherapy.

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