

EMA/576787/2020

## European Medicines Agency decision

P/0432/2020

of 5 November 2020

on the acceptance of a modification of an agreed paediatric investigation plan for nivolumab (Opdivo), (EMA-001407-PIP01-12-M03) 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<sup>1</sup>,

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<sup>2</sup>,

Having regard to the European Medicines Agency's decision P/0064/2014 issued on 7 March 2014, the decision P/0049/2018 issued on 22 February 2018 and the decision P/0026/2020 issued on 9 January 2020,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 10 July 2020 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 October 2020, 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.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> 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, 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 Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, D15 T867 - Dublin 15, Ireland.

EMA/PDCO/417355/2020  
Amsterdam, 16 October 2020

## Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-001407-PIP01-12-M03

### 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

## **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 10 July 2020 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 decision P/0049/2018 issued on 22 February 2018 and the decision P/0026/2020 issued on 9 January 2020.

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

The procedure started on 18 August 2020.

## **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 and to the deferral 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, 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 of age
- Treatment of patients with unresectable or metastatic melanoma in the age group from 12 to less than 18 years 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 studies | Description                                                                |
|-------------------------|-------------------|----------------------------------------------------------------------------|
| Quality-related studies | 0                 | Not applicable                                                             |
| Non-clinical studies    | 1                 | <b>Study 1</b><br>Non-clinical biomarker study in paediatric tumour tissue |

|                                               |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----------------------------------------------|---|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Clinical studies                              | 2 | <p><b>Study 2</b></p> <p>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 (CA209070)</p> <p><b>Study 3</b> deleted in procedure EMEA-001407-PIP01-12-M03</p> |
| Extrapolation, modelling & simulation studies | 1 | <p><b>Study 4</b></p> <p>Study to generate paediatric dosing recommendations for nivolumab alone and in combination with ipilimumab</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| 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 February 2022 |
| 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. 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 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 locally advanced or metastatic non-small cell lung cancer after prior chemotherapy 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 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.

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