EMA/28103/2018

European Medicines Agency decision

P/0008/2018

of 30 January 2018

on the acceptance of a modification of an agreed paediatric investigation plan for pembrolizumab (Keytruda), (EMEA-001474-PIP02-16-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/0204/2016 issued on 1 August 2016,

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc on 25 September 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 15 December 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.

[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 pembrolizumab (Keytruda), concentrate for solution for infusion, powder for 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/0059/2014 issued on 7 March 2014, including subsequent modifications thereof.

Article 3

This decision is addressed to Merck Sharp & Dohme (Europe), Inc., Clos du Lynx 5, Binnenhof, B-1200 Brussels, Belgium.

EMA/PDCO/661223/2017
London, 15 December 2017

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

EMEA-001474-PIP02-16-M01

Scope of the application

Active substance(s):

Pembrolizumab

Invented name:

Keytruda

Condition(s):

Treatment of Hodgkin lymphoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Powder for concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Merck Sharp & Dohme (Europe), Inc

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, Merck Sharp & Dohme (Europe), Inc submitted to the European Medicines Agency on 25 September 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/0204/2016 issued on 1 August 2016.

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

The procedure started on 17 October 2017.

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 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 Hodgkin lymphoma

The waiver applies to:

- the paediatric population from birth to less than 3 years of age;
- concentrate for solution for infusion and powder for concentrate for solution, 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 Hodgkin lymphoma

2.1.1. Indication(s) targeted by the PIP

- Treatment of classical Hodgkin lymphoma with incomplete early response to front-line chemotherapy in children from 3 years to less than 18 years of age
- Treatment of relapsed or refractory classical Hodgkin lymphoma in children from 5 years to less than 18 years of age

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

From 3 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

- Concentrate for solution for infusion
- Powder for 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** Multi-centre, open-label, single-arm trial to evaluate pharmacokinetics, pharmacodynamics, toxicity, safety and activity of pembrolizumab in paediatric patients from 6 months to less than 18 years with an advanced melanoma or a PD-L1 positive advanced, relapsed or refractory solid tumour or lymphoma, including an expansion phase (same as study 2 in EMEA-001474-PIP01-13) **Study 2** Open-label, non-controlled trial to evaluate the safety and efficacy of pembrolizumab in combination with chemotherapy in paediatric patients from 3 years to less than 18 years of age (and young adults) with a classical Hodgkin with incomplete early response to front-line therapy
Extrapolation, modelling & simulation studies	0	Not applicable.
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 January 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 Hodgkin lymphoma

Authorised indication(s):

- KEYTRUDA as monotherapy is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) who have failed autologous stem cell transplant(ASCT) and brentuximab vedotin (BV), or who are transplant-ineligible and have failed BV.

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

Authorised indication(s):

- KEYTRUDA as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.
- KEYTRUDA as monotherapy is indicated for the first-line treatment of metastatic non-small cell lung carcinoma (NSCLC) in adults whose tumours express PD-L1 with a ≥50% tumour proportion score(TPS) with no EGFR or ALK positive tumour mutations.
- KEYTRUDA as monotherapy is indicated for the treatment of locally advanced or metastatic NSCLC in adults whose tumours express PD-L1 with a ≥1% TPS and who have received at least one prior chemotherapy regimen. Patients with EGFR or ALK positive tumour mutations should also have received targeted therapy before receiving KEYTRUDA.
- KEYTRUDA as monotherapy is indicated for the treatment of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy.
- KEYTRUDA as monotherapy is indicated for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy.

Authorised pharmaceutical form(s):

Powder for concentrate for solution for infusion

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use