EMA/395100/2019

European Medicines Agency decision

P/0276/2019

of 14 August 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for vedolizumab (Entyvio) (EMEA-000645-PIP03-18) 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 application submitted by Takeda Pharma A/S on 6 September 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 28 June 2019, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for vedolizumab (Entyvio), powder for concentrate for solution for infusion, solution for injection, intravenous use, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for vedolizumab (Entyvio), powder for concentrate for solution for infusion, solution for injection, intravenous use, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for vedolizumab (Entyvio), powder for concentrate for solution for infusion, solution for injection, intravenous use, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/145/2010 issued on 30 July 2010, including subsequent modifications thereof.

Article 5

This decision is addressed to Takeda Pharma A/S, Dybendal Alle 10, 2630 – Taastrup, Denmark.

EMA/PDCO/210935/2019
Amsterdam, 28 June 2019

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-000645-PIP03-18

Scope of the application

Active substance(s):

Vedolizumab

Invented name:

Entyvio

Condition(s):

Prevention of acute graft-versus-host disease

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for concentrate for solution for infusion

Solution for injection

Route(s) of administration:

Intravenous use

Subcutaneous use

Name/corporate name of the PIP applicant:

Takeda Pharma A/S

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Takeda Pharma A/S submitted for agreement to the European Medicines Agency on 6 September 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 16 October 2018.

Supplementary information was provided by the applicant on 25 March 2019. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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:

Prevention of acute graft-versus-host disease

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- powder for concentrate for solution for infusion, solution for injection; intravenous use, subcutaneous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Prevention of acute graft-versus-host disease

2.1.1. Indication(s) targeted by the PIP

Prophylaxis for intestinal acute graft-versus-host disease in patients who are planned to undergo allogeneic hematopoietic stem cell transplantation

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

From 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of age-appropriate presentation of powder for concentrate for solution for infusion
Non-clinical studies	0	Not applicable

Clinical studies	2	**Study 2** Double-blind, randomised, placebo-controlled study to evaluate efficacy and safety of vedolizumab as add-on to standard of care as prophylaxis for intestinal acute graft-versus-host disease (aGvHD) in adolescents from 12 to less than 18 years of age (and adults) planned to undergo allogeneic haematopoietic stem cell transplantation (allo-HSCT) **Study 3** Open-label, uncontrolled study to evaluate pharmacokinetics, immunogenicity, efficacy, safety and tolerability of vedolizumab as add-on to standard of care as prophylaxis for intestinal acute graft-versus-host disease (aGvHD) in children from 28 days to less than 18 years of age planned to undergo allogeneic haematopoietic stem cell transplantation (allo-HSCT)
Extrapolation, modelling and simulation studies	2	**Study 4** Modelling and simulation study to evaluate the use of vedolizumab as prophylaxis for intestinal acute graft-versus-host disease (aGvHD) in children from 28 days to less than 18 years of age undergoing allogeneic haematopoietic stem cell transplantation (allo-HSCT) **Study 5** Extrapolation study to evaluate the use of vedolizumab as prophylaxis for intestinal acute graft-versus-host disease (aGvHD) in children from 28 days to less than 18 years of age undergoing allogeneic haematopoietic stem cell transplantation (allo-HSCT)
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:	No
Date of completion of the paediatric investigation plan:	By July 2027
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 Crohn's disease

Authorised indication(s):

- Treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist.

2. Treatment of ulcerative colitis

Authorised indication(s):

- Treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist.

Authorised pharmaceutical form(s):

Powder for concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use