EMA/197922/2018

European Medicines Agency decision

P/0109/2018

of 11 April 2018

on the acceptance of a modification of an agreed paediatric investigation plan for vedolizumab (Entyvio), (EMEA-000645-PIP01-09-M06) 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

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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/145/2010 issued on 30 July 2010, the decision P/0053/2013 issued on 20 March 2013, the decision P/0317/2014 issued on 12 December 2014, and the decision P/0015/2016 issued on 29 January 2016 and the decision P/0247/2016 issued on 13 September 2016 and the decision P/0146/20017 issued on 7 June 2017,

Having regard to the application submitted by Takeda Pharma A/S on 8 December 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 23 February 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 and to the waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the 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

Changes to the agreed paediatric investigation plan for vedolizumab (Entyvio), powder for concentrate for solution for infusion, solution for injection in pre-filled syringe, intravenous use, subcutaneous use, including changes to the waiver, 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 Takeda Pharma A/S, Dybendall Alle 10, 2630 – Taastrup, Denmark.

EMA/PDCO/829985/2017 Corr
London, 23 February 2018

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

EMEA-000645-PIP01-09-M06

Scope of the application

Active substance(s):

Vedolizumab

Invented name:

Entyvio

Condition(s):

Treatment of Crohn's disease

Treatment of ulcerative colitis

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for concentrate for solution for infusion

Solution for injection in pre-filled syringe

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

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, Takeda Pharma A/S submitted to the European Medicines Agency on 8 December 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/145/2010 issued on 30 July 2010, the decision P/0053/2013 issued on 20 March 2013, the decision P/0317/2014 issued on 12 December 2014, the decision P/0015/2016 issued on 29 January 2016 and the decision P/0247/2016 issued on 13 September 2016 and the decision P/0146/2017 issued on 7 June 2017.

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

The procedure started on 3 January 2018.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified. A waiver for a paediatric subset has been removed.

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 waiver 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 Crohn's disease

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- powder for concentrate for solution for infusion, intravenous use; solution for injection in pre-filled syringe, subcutaneous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1.2. Condition:

Treatment of ulcerative colitis

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- powder for concentrate for solution for infusion, intravenous use; solution for injection in pre-filled syringe, subcutaneous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of Crohn's disease

2.1.1. Indication(s) targeted by the PIP

Treatment of moderately to severely active Crohn’s disease

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

Solution for injection in pre-filled syringe

2.1.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable
Non-clinical	0	Not applicable
Clinical	4	**Study 1 (MLN0002-2003)** Randomised, double-blind, dose-ranging clinical pharmacology study to determine the pharmacokinetics, safety and tolerability of vedolizumab in paediatric patients with Ulcerative Colitis or Crohn's Disease **Study 2 (MLN0002-3025)** Randomised, double-blind, placebo-controlled two-dose, three-arm, multicentre study of the induction and maintenance of clinical response and remission by vedolizumab in paediatric patients with moderate to severe Crohn's disease **Study 4** (added during procedure EMEA-000645-PIP01-09-M06) A substudy to long-term extension study (Vedolizumab-2005 IV OLE) to determine the pharmacokinetics (PK), immunogenicity, safety, and tolerability of vedolizumab subcutaneous use (SC) in paediatric subjects with ulcerative colitis or Crohn's disease **Study 5** (added during procedure EMEA-000645-PIP01-09-M06) Open-Label study to determine the pharmacokinetics, efficacy and long-term safety of vedolizumab subcutaneous use (SC) in paediatric subjects with ulcerative colitis or Crohn's disease
Extrapolation, modelling and simulation studies	1	**Study 6** (added during procedure EMEA-000645-PIP01-09-M06) Modelling and simulation study to evaluate use of vedolizumab via the subcutaneous route in children and adolescents from 2 years to less than 18 years with ulcerative colitis or Crohn's disease
Other studies	0	Not applicable
Other measures	0	Not applicable

2.2. Condition:

Treatment of ulcerative colitis

2.2.1. Indication(s) targeted by the PIP

Treatment of moderately to severely active ulcerative colitis

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

From 2 to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

Solution for injection in pre-filled syringe

2.2.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable
Non-clinical	0	Not applicable
Clinical	4	**Study 1 (MLN0002-2003)** The same as for treatment of Crohn's disease **Study 3 (MLN0002-3024)** Randomised, double-blind, placebo-controlled two-dose, three-arm, multicentre study of the induction and maintenance of clinical response and remission by vedolizumab in paediatric patients with moderate to severe ulcerative colitis **Study 4** (added during procedure EMEA-000645-PIP01-09-M06) The same as for treatment of Crohn's disease **Study 5** (added during procedure EMEA-000645-PIP01-09-M06) The same as for treatment of Crohn's disease
Extrapolation, modelling and simulation studies	1	Study 6 (added during procedure EMEA-000645-PIP01-09-M06) The same as for treatment of Crohn's disease
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 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 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.

2. 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.

Authorised pharmaceutical form(s):

Powder for concentrate for solution

Authorised route(s) of administration:

Intravenous use