EMA/319200/2024

European Medicines Agency decision

P/0244/2024

of 18 July 2024

on the acceptance of a modification of an agreed paediatric investigation plan for vedolizumab (Entyvio), (EMEA-000645-PIP01-09-M09) 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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on the acceptance of a modification of an agreed paediatric investigation plan for vedolizumab (Entyvio), (EMEA-000645-PIP01-09-M09) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Union procedures for the authorisation and supervision of medicinal products for human 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, the decision P/0015/2016 issued on 29 January 2016, the decision P/0247/2016 issued on 13 September 2016, the decision P/0146/20017 issued on 7 June 2017, the decision P/0109/2018 issued on 11 April 2018, the decision P/0361/2020 issued on 5 October 2020, and the decision P/0552/2021 issued on 31 December 2021,

Having regard to the application submitted by Takeda Pharma A/S on 23 February 2024 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 31 May 2024, 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.

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

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, intravenous use subcutaneous 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 Takeda Pharma A/S, Delta Park 45, 2665 - Vallensbaek Strand, Denmark.

EMA/PDCO/89968/2024 Corr[1]
Amsterdam, 31 May 2024

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

EMEA-000645-PIP01-09-M09

Scope of the application

Active substance(s):

Vedolizumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of Crohn's disease

Treatment of ulcerative colitis

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

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 22 February 2024 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

[1] 12 July 2024

issued on 29 January 2016, the decision P/0247/2016 issued on 13 September 2016, the decision P/0146/20017 issued on 7 June 2017, the decision P/0109/2018 issued on 11 April 2018, the decision P/0361/2020 issued on 5 October 2020, and the decision P/0552/2021 issued on 31 December 2021.

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

The procedure started on 2 April 2024.

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.
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 of age;
- powder for concentrate for solution for infusion, intravenous use; solution for injection, 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 of age;
- powder for concentrate for solution for infusion, intravenous use; solution for injection, 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

2.1.4. Measures

Area	Description
Quality	Not applicable

Non-clinical	Not applicable
Clinical	**Study 1 (MLN0002-2003)** Randomised, double-blind, dose-ranging clinical pharmacology study to determine the pharmacokinetics, safety and tolerability of vedolizumab in paediatric subjects from 2 years to less than 18 years of age with ulcerative colitis or Crohn's disease **Study 2 (MLN0002-3025)** Randomised, double-blind, multicentre study comparing two doses to evaluate the efficacy and safety of vedolizumab intravenous as maintenance therapy in paediatric subjects from 2 years to less than 18 years of age with moderately to severely active Crohn's disease who achieved clinical response following open-label vedolizumab intravenous therapy **Study 4** (deleted during procedure EMEA-000645-PIP01-09-M08) **Study 5 (VedolizumabSC-3003)** (added during procedure EMEA-000645-PIP01-09-M06) Open-label study to determine the pharmacokinetics, safety and immunogenicity of vedolizumab subcutaneous use (SC) in paediatric subjects from 2 years to less than 18 years of age with ulcerative colitis or Crohn's disease
Extrapolation, modelling and simulation studies	**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 of age with ulcerative colitis or Crohn's disease
Other studies	Not applicable
Other measures	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	Description
Quality	Not applicable
Non-clinical	Not applicable
Clinical	**Study 1 (MLN0002-2003)** The same as for treatment of Crohn's disease **Study 3 (MLN0002-3024)** Randomised, double-blind, multicentre study comparing two doses to evaluate the efficacy, safety and pharmacokinetics of vedolizumab intravenous as maintenance therapy in paediatric subjects from 2 years to less than 18 years of age with moderately to severely active ulcerative colitis who achieved clinical response following open-label vedolizumab intravenous therapy **Study 4** (deleted during procedure EMEA-000645-PIP01- 09-M08) The same as for treatment of Crohn's disease **Study 5 (VedolizumabSC-3003)** (added during procedure EMEA-000645-PIP01- 09-M06) The same as for treatment of Crohn's disease
Extrapolation, modelling and simulation studies	**Study 6** (added during procedure EMEA-000645-PIP01-09-M06) The same as for treatment of Crohn's disease
Other studies	Not applicable
Other measures	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 September 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

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
- Invented name(s):

  Entyvio 300 mg powder for concentrate for solution for infusion

  Entyvio 108 mg solution for injection in pre-filled syringe

  Entyvio 108 mg solution for injection in pre-filled pen
- Authorised pharmaceutical form(s):

  Powder for concentrate for solution for infusion

  Solution for injection (injection)
- Authorised route(s) of administration:

  Entyvio 300 mg powder for concentrate for solution for infusion is for intravenous use only.
- Entyvio solution for injection (in a pre-filled syringe or a pre-filled pen) is for subcutaneous injection only. Authorised via centralised procedure

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
- Invented name(s)

  Entyvio 300 mg powder for concentrate for solution for infusion

  Entyvio 108 mg solution for injection in pre-filled syringe

  Entyvio 108 mg solution for injection in pre-filled pen
- Authorised pharmaceutical form(s):

  Powder for concentrate for solution for infusion

  Solution for injection (injection)
- Authorised route(s) of administration:

  Entyvio 300 mg powder for concentrate for solution for infusion is for intravenous use only.

  Entyvio solution for injection (in a pre-filled syringe or a pre-filled pen) is for subcutaneous injection only
- Authorised via centralised procedure

3. Treatment of pouchitis

Authorised indication(s):

- Entyvio is indicated for the treatment of adult patients with moderately to severely active chronic pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis, and have had an inadequate response with or lost response to antibiotic therapy
- Invented name(s)

  Entyvio 300 mg powder for concentrate for solution for infusion
- Authorised pharmaceutical form(s):

  Powder for concentrate for solution for infusion
- Authorised route(s) of administration:

  Entyvio 300 mg powder for concentrate for solution for infusion is for intravenous use only
- Authorised via centralised procedure