EMA/709431/2022

European Medicines Agency decision

P/0401/2022

of 9 September 2022

on the acceptance of a modification of an agreed paediatric investigation plan for ustekinumab (Stelara), (EMEA-000311-PIP04-13-M05) 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 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/0045/2014 issued on 7 March 2014, the decision P/0096/2019 issued on 22 March 2019, the decision P/0321/2020 issued on 12 August 2020 and the decision P/0083/2021 issued on 19 March 2021,

Having regard to the application submitted by Janssen-Cilag International NV on 22 April 2022 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 22 July 2022, 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 and 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 ustekinumab (Stelara), solution for injection, concentrate for solution for infusion, subcutaneous use, 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0190/2018 issued on 17 July 2018, P/19/2009 issued on 4 February 2009 and P/0062/2012 issued on 28 March 2012 including subsequent modifications thereof.

Article 3

This decision is addressed to Janssen-Cilag International NV, Turnhoutseweg 30, B2340 – Beerse, Belgium.

EMA/PDCO/250513/2022
Amsterdam, 22 July 2022

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

EMEA-000311-PIP04-13-M05

Scope of the application

Active substance(s):

Ustekinumab

Invented name:

Stelara

Condition(s):

Treatment of Crohn's disease

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Concentrate for solution for infusion

Route(s) of administration:

Subcutaneous use

Intravenous use

Name/corporate name of the PIP applicant:

Janssen-Cilag International NV

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted to the European Medicines Agency on 22 April 2022 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/0045/2014 issued on 7 March 2014, the decision P/0096/2019 issued on 22 March 2019, the decision P/0321/2020 issued on 12 August 2020 and the decision P/0083/2021 issued on 19 March 2021.

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

The procedure started on 23 May 2022.

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 Paediatric Committee member of Norway 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 of age;
- solution for injection, subcutaneous use; concentrate for solution for infusion, intravenous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of Crohn's disease

2.1.1. Indication(s) targeted by the PIP

Treatment of 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)

Solution for injection

Concentrate for solution for infusion

2.1.4. Measures

Area	Description
Quality studies	**Study 1** Deleted during procedure EMEA-000311-PIP04-13-M03
Non-clinical studies	Not applicable
Clinical studies	**Study 2 - CNTO1275PCRD1001** Randomized, double-blind, pharmacokinetic (PK) study of intravenous (IV) ustekinumab induction followed by subcutaneous (SC) ustekinumab maintenance in children and adolescents 2 to less than 18 years (6 to less than 18 years in the EU) with moderately to severely active Crohn's disease (CD) who have had an inadequate response and/or intolerance to conventional therapies

	Study 3 - CNTO1275CRD3004 Open-label single administration of IV induction dose of ustekinumab followed by a randomized, double-blind, 2-arm study of two different SC ustekinumab maintenance dose regimens to assess the pharmacokinetics, safety and clinical response in children and adolescents 2 to less than 18 years with moderately to severely active Crohn's disease who have had an inadequate response and/or intolerance to biologic therapy and/or conventional therapies **Study 7** Added during procedure EMEA-000311-PIP04-13-M05 Retrospective, single-arm, non-interventional, observational, real-world evidence study to evaluate the effectiveness of ustekinumab by estimating clinical remission at week 52 since initiation of ustekinumab in children and adolescents from 2 years to less than 18 years of age with moderately to severely active Crohn's disease.
Extrapolation, modelling and simulation studies	**Study 4** Added during procedure EMEA-000311-PIP04-13-M01 Population PK model **Study 5** Added during procedure EMEA-000311-PIP04-13-M01 Exposure-response model **Study 6** Added during procedure EMEA-000311-PIP04-13-M01 Analysis of internal and literature data to support the assumptions of similarity of disease, treatment effects, and exposure-response relationship between paediatric and adult subjects with Crohn's disease (CD)
Other studies	Not applicable
Other measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By January 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 plaque psoriasis

Authorised indication(s):

- Stelara is indicated for the treatment of moderate to severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or PUVA (psoralen and ultraviolet A) (see section 5.1).

  Paediatric plaque psoriasis

- Stelara is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescent patients from the age of 6 years and older, who are inadequately controlled by, or are 20 intolerant to, other systemic therapies or phototherapies (see section 5.1).

2. Treatment of psoriatic arthritis

Authorised indication(s):

- Stelara alone or in combination with MTX, is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous non-biological disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate.

3. Treatment of Crohn's disease

- Stelara is indicated for the 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 TNFα antagonist or have medical contraindications to such therapies.

4. Treatment of ulcerative colitis

- Stelara is indicated for the 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 biologic or have medical contraindications to such therapies (see section 5.1).

Authorised pharmaceutical form(s):

Solution for injection

Authorised route(s) of administration:

Subcutaneous use