

EMA/122313/2019

European Medicines Agency decision

P/0096/2019

of 22 March 2019

on the acceptance of a modification of an agreed paediatric investigation plan for ustekinumab (Stelara), (EMEA-000311-PIP04-13-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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/0045/2014 issued on 7 March 2018,

Having regard to the application submitted by Janssen-Cilag International NV on 29 October 2018 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 1 February 2019, 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 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 deferral and 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 ustekinumab (Stelara), solution for injection, concentrate for solution for infusion, subcutaneous use, intravenous use, including changes to the deferral and 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 Janssen-Cilag International NV, Turnhoutseweg 30, B2340 – Beerse, Belgium.

EMA/PDCO/789813/2018
London, 1 February 2019

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan 000311-PIP04-13-M01

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 29 October 2018 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 2018.

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

The procedure started on 4 December 2018.

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 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;
- solution for injection for subcutaneous use; for concentrate for solution for infusion, for 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	Number of measures	Description
Quality studies	1	Study 1 Development of prefilled syringe for subcutaneous (SC) administration with age-appropriate strength
Non-clinical studies	0	N/A
Clinical studies	2	Study 2 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 (CNT01275CRD1001)

		Study 3 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 conventional therapies
Extrapolation, modelling and simulation studies	3	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	0	Not applicable
Other measures	0	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 December 2023
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 adolescent patients from the age of 12 years and older, who are inadequately controlled by, or are 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 TNF α antagonist or have medical contraindications to such therapies.

Authorised pharmaceutical form(s):

Solution for injection

Authorised route(s) of administration:

Subcutaneous use