EMA/762538/2018

European Medicines Agency decision

P/0394/2018

of 7 December 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for upadacitinib (EMEA-001741-PIP04-17) 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 AbbVie Ltd on 18 December 2017 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 19 October 2018, 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 upadacitinib, prolonged-release tablet, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral 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 upadacitinib, prolonged-release tablet, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral 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 upadacitinib, prolonged-release tablet, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral 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 is addressed to AbbVie Ltd, AbbVie House, Vanwall Road, SL6 4UB - Maidenhead, United Kingdom.

EMA/PDCO/500295/2018
London, 19 October 2018

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

EMEA-001741-PIP04-17

Scope of the application

Active substance(s):

Upadacitinib

Condition(s):

Treatment of atopic dermatitis

Pharmaceutical form(s):

Prolonged-release tablet

Age-appropriate oral solid dosage form

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

AbbVie Ltd

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Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AbbVie Ltd submitted for agreement to the European Medicines Agency on 18 December 2017 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 23 January 2018.

Supplementary information was provided by the applicant on 16 July 2018. The applicant proposed modifications to the paediatric investigation plan.

A meeting with the Paediatric Committee took place on 18 October 2018.

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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all 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 annex 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 atopic dermatitis

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- prolonged-release tablet, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of atopic dermatitis

2.1.1. Indication(s) targeted by the PIP

Treatment of moderate to severe atopic dermatitis in children from 2 years of age who are candidates for systemic therapy

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)

Prolonged-release tablet

Age-appropriate oral solid dosage form

Age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of age-appropriate oral solid dosage form (dispersible tablet or multi-particulate granules) or age-appropriate oral liquid dosage form
Non-clinical studies	2	**Study 2** Dose range-finding juvenile toxicity study

		Study 3 Definitive juvenile toxicity study to evaluate toxicity and impact of upadacitinib on neonatal/juvenile development
Clinical studies	6	**Study 4** Open-label, multiple-dose trial to evaluate activity, safety and tolerability (Part 1) and long-term safety and tolerability (Part 2) of upadacitinib in children from 2 to less than 12 years of age with severe atopic dermatitis (AD) **Study 5** Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of upadacitinib in adolescents (and adults) with moderate to severe AD who are candidates for systemic therapy (M16-045) **Study 6** Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of upadacitinib in adolescents (and adults) with moderate to severe AD who are candidates for systemic therapy in combination with topical corticosteroids (M16-047) **Study 7** Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of upadacitinib in adolescents (and adults) with moderate to severe AD who are candidates for systemic therapy (M18-891) **Study 8** Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of upadacitinib as add-on to standard of care in children from 2 to less than 18 years of age with severe AD **Study 9** Open-label, extension study to evaluate long-term safety and efficacy of upadacitinib monotherapy in children from 2 to less than 18 years of age with severe atopic dermatitis
Extrapolation, modelling and simulation studies	2	**Study 10** PopPK to predict initial paediatric doses to be used in further clinical studies PopPK to confirm or modify the paediatric posology compared to the regimen used in clinical trials **Study 11** Population exposure response analyses to identify subgroups where this relationship is altered and may need posology changes or other risk mitigation measures selection
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 May 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes