EMA/192364/2021

European Medicines Agency decision

P/0166/2021

of 14 April 2021

on the acceptance of a modification of an agreed paediatric investigation plan for upadacitinib (Rinvoq), (EMEA-001741-PIP04-17-M02) 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 European Medicines Agency's decision P/0394/2018 issued on 7 December 2018 and the decision P/0214/2020 issued on 17 June 2020,

Having regard to the application submitted by AbbVie Ltd on 27 November 2020 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 26 February 2021, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for upadacitinib (Rinvoq), prolonged-release tablet, prolonged-release capsule, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral 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/0288/2015 issued on 27 November 2015, including subsequent modifications thereof.

Article 3

This decision is addressed to AbbVie Ltd, AbbVie House, Vanwall Road, SL6 4UB – Maidenhead, United Kingdom.

EMA/PDCO/656667/2020
Amsterdam, 26 February 2021

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

EMEA-001741-PIP04-17-M02

Scope of the application

Active substance(s):

Upadacitinib

Invented name:

Rinvoq

Condition(s):

Treatment of atopic dermatitis

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Prolonged-release tablet

Prolonged-release capsule

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

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, AbbVie Ltd submitted to the European Medicines Agency on 27 November 2020 an application for modification of the agreed paediatric investigation with a deferral and a waiver as set out in the European Medicines Agency's decision P/0394/2018 issued on 7 December 2018 and the decision P/0214/2020 issued on 17 June 2020.

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

The procedure started on 4 January 2021.

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 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 atopic dermatitis

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- prolonged-release tablet, prolonged-release capsule, 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

Prolonged-release capsule

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 November 2024
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 rheumatoid arthritis

Authorised indication(s):

Rinvoq is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). Rinvoq may be used as monotherapy or in combination with methotrexate.

Authorised pharmaceutical form(s):

Prolonged-release tablet

Authorised route(s) of administration:

Oral use