EMA/89850/2024

European Medicines Agency decision

P/0079/2024

of 8 March 2024

on the acceptance of a modification of an agreed paediatric investigation plan for upadacitinib (Rinvoq), (EMEA-001741-PIP04-17-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/0394/2018 issued on 7 December 2018, the decision P/0214/2020 issued on 17 June 2020 and the decision P/0166/2021 issued on 14 April 2021,

Having regard to the application submitted by AbbVie Ltd on 13 October 2023 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 19 January 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 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/501089/2023
Amsterdam, 19 January 2024

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

EMEA-001741-PIP04-17-M05

Scope of the application

Active substance(s):

Upadacitinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of atopic dermatitis

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

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, AbbVie Ltd submitted to the European Medicines Agency on 13 October 2023 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/0394/2018 issued on 7 December 2018, the decision P/0214/2020 issued on 17 June 2020 and the decision P/0166/2021 issued on 14 April 2021.

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

The procedure started on 20 November 2023.

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 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	Description
Quality-related studies	**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	**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	**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** Open-label, randomised, assessor-blinded, dupilumab-controlled trial to evaluate safety and efficacy of upadacitinib in children from 2 years to less than 12 years of age with moderate to severe AD (M17-380) **Study 9** *Deleted during procedure EMEA-001741-PIP04-17-M05.*
Extrapolation, modelling and simulation studies	**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	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 March 2030
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 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.
  - Invented name(s): Rinvoq
  - Authorised pharmaceutical form(s): prolonged-release tablet
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure

2. Treatment of psoriatic arthritis

Authorised indication(s):

- Rinvoq is indicated for the treatment of active psoriatic arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more DMARDs. RINVOQ may be used as monotherapy or in combination with methotrexate. Invented name(s): Rinvoq
  - Authorised pharmaceutical form(s): prolonged-release tablet
  - Authorised route(s) of administration: oral
  - Authorised via centralised procedure

3. Treatment of axial spondyloarthritis

Authorised indication(s):

Non-radiographic axial spondyloarthritis (nr-axSpA)

- Rinvoq is indicated for the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI), who have responded inadequately to nonsteroidal anti-inflammatory drugs (NSAIDs).

Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)

- Rinvoq is indicated for the treatment of active ankylosing spondylitis in adult patients who have responded inadequately to conventional therapy.
  - Invented name(s): Rinvoq
  - Authorised pharmaceutical form(s): prolonged-release tablet
  - Authorised route(s) of administration: oral
  - Authorised via centralised procedure

4. Treatment of atopic dermatitis

Authorised indication(s):

- Rinvoq is indicated for the treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.
  - Invented name(s): Rinvoq
  - Authorised pharmaceutical form(s): prolonged-release tablet
  - Authorised route(s) of administration: oral
  - Authorised via centralised procedure

5. Treatment of ulcerative colitis

Authorised indication(s):

- Rinvoq is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent.
  - Invented name(s): Rinvoq
  - Authorised pharmaceutical form(s): prolonged-release tablet
  - Authorised route(s) of administration: oral
  - Authorised via centralised procedure

6. Treatment of Crohn’s disease

Authorised indication(s):

- RINVOQ is indicated for the treatment of adult patients with moderately to severely active Crohn’s disease who have had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent.
  - Invented name(s): Rinvoq
  - Authorised pharmaceutical form(s): prolonged-release tablet
  - Authorised route(s) of administration: oral
  - Authorised via centralised procedure