

EMA/486034/2023

European Medicines Agency decision P/0452/2023

of 31 October 2023

on the acceptance of a modification of an agreed paediatric investigation plan for upadacitinib (Rinvoq), (EMEA-001741-PIP03-16-M04) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency²,

Having regard to the European Medicines Agency's decision P/0046/2018 issued on 16 February 2018, the decision P/0069/2019 issued on 22 March 2019, the decision P/0198/2022 issued on 2 June 2022 and the decision P/0263/2022 issued on 13 July 2022.

Having regard to the application submitted by AbbVie Ltd on 3 July 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 13 October 2023, 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), age-appropriate oral pharmaceutical form, prolonged-release tablet, 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, P/0394/2018 issued on 7 December 2018 and P/0022/2018 issued on 30 January 2018, including subsequent modifications thereof.

Article 3

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

EMA/PDCO/315764/2023
Amsterdam, 13 October 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-001741-PIP03-16-M04

Scope of the application

Active substance(s):

Upadacitinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of Crohn's disease

Pharmaceutical form(s):

Age-appropriate oral pharmaceutical form

Prolonged-release tablet

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 3 July 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/0046/2018 issued on 16 February 2018, the decision P/0069/2019 issued on 22 March 2019, the decision P/0198/2022 issued on 2 June 2022 and the decision P/0263/2022 issued on 13 July 2022.

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

The procedure started on 14 August 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 Crohn's disease

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- prolonged-release tablet, age-appropriate oral pharmaceutical form, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of Crohn's disease (CD)

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with moderately to severely active Crohn's disease

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Prolonged-release tablet

Age-appropriate oral pharmaceutical form

2.1.4. Measures

Area	Description
Quality-related studies	Study 1 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 - M14-671 Double-blind safety, efficacy, and pharmacokinetic study with an open label induction phase of upadacitinib in children from 2 to less than 18 years with moderately to severely active Crohn's disease, who have had an inadequate response or been intolerant to corticosteroids, immunosuppressants, and/or biologic therapy, or have medical contraindications to such therapies
Extrapolation, modelling and simulation studies	Study 5 Population PK modelling and simulation study to determine the dose of upadacitinib in children from 2 to less than 18 years of age with Crohn's disease
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:	No
Date of completion of the paediatric investigation plan:	By September 2032
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. Condition: Treatment of Chronic Idiopathic Arthritis (including rheumatoid arthritis, psoriatic arthritis, spondyloarthritis and juvenile idiopathic arthritis)

Authorised indications:

- 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.
- 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 use;
 - Authorised via centralised procedure.
- 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).
 - Invented name(s): Rinvoq;
 - Authorised pharmaceutical form(s): prolonged-release tablet;
 - Authorised route(s) of administration: oral use;
 - Authorised via centralised procedure.
- 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 use;
 - Authorised via centralised procedure.

2. Condition: Treatment of atopic dermatitis

Authorised indication:

- 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 use;
- Authorised via centralised procedure.

3. Condition: Treatment of Ulcerative Colitis

Authorised indication:

- 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 use;
- Authorised via centralised procedure.

4. Condition: Treatment of Crohn's disease

Authorised indication:

- 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 use;
- Authorised via centralised procedure.