EMADOC-1700519818-1855380

European Medicines Agency decision

EMA/PE/0000226303

of 28 January 2025

on the acceptance of a modification of an agreed paediatric investigation plan for naldemedine tosilate (Rizmoic), 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/0312/2016 issued on 11 November 2016, the decision P/0044/2017 issued on 17 February 2017 and the decision P/0379/2021 issued on 8 September 2021,

Having regard to the application submitted by Shionogi B.V. on 30 August 2024 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 December 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 naldemedine tosilate (Rizmoic), 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 is addressed to Shionogi B.V., Herengracht 464, 1017 CA - Amsterdam, Netherlands.

EMADOC-1700519818-1706154
Amsterdam, 13 December 2024

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

EMA/PE/0000226303

Scope of the application

Active substance(s):

Naldemedine (tosilate)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of opioid-induced constipation

Pharmaceutical form(s):

Tablet

Powder for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Shionogi B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Shionogi B.V. submitted to the European Medicines Agency on 30 August 2024 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/0312/2016 issued on 11 November 2016, the decision P/0044/2017 issued on 17 February 2017 and the decision P/0379/2021 issued on 8 September 2021.

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

The procedure started on 14 October 2024.

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 members of Liechtenstein and Norway agree 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 opioid induced constipation

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- tablet, powder for oral suspension; oral use;
- on the grounds that the specific medicinal product is likely to be unsafe,

and

- the paediatric population from 6 months to less than 2 years of age;
- tablet, powder for oral suspension; oral 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 opioid induced constipation

2.1.1. Indication(s) targeted by the PIP

Treatment of opioid induced constipation (OIC)

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)

Tablet.

Powder for oral suspension.

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age appropriate powder for oral suspension for oral use.
Non-clinical studies	**Study 2** Dose range-finding juvenile toxicity study. **Study 3**

	Definitive juvenile toxicity study.
Clinical studies	**Study 4** Open-label study to assess the pharmacokinetics, safety, and tolerability of naldemedine in paediatric patients who are receiving or who are about to receive treatment with opioids from 2 years of age to less than 18 years old (V921F).
Extrapolation, modelling and simulation studies	**Study 5** Population pharmacokinetic modeling and simulation study. **Study 6** Extrapolation of efficacy of naldemedine from adults to the paediatric population.
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 2026
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 opioid-induced constipation

Authorised indication(s):

- Rizmoic is indicated for the treatment of opioid-induced constipation (OIC) in adult patients who have previously been treated with a laxative.
  - Invented name(s): Rizmoic
  - Authorised pharmaceutical form(s): film-coated tablet
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure