MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100325-PIP01-21-M01

Scope of the Application

Active Substance(s)

NALDEMEDINE

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 the Decision

Pursuant to the Human Medicines Regulations 2012, Shionogi B.V. submitted to the licensing authority on 09/11/2021 16:00 GMT an application for a Modification

The procedure started on 10/08/2022 17:43 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100325-PIP01-21-M01

Of 06/09/2022 16:18 BST

On the adopted decision for NALDEMEDINE (MHRA-100325-PIP01-21-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for NALDEMEDINE, Tablet; Powder for oral suspension , Oral use .

This decision is addressed to Shionogi B.V., 33 Kingsway, Holborn, London, United Kingdom, WC2B 6UF

ANNEX I

1. Waiver

1.1 Condition:

Treatment of opioid-induced constipation The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Tablet; Powder for oral suspension. Route(s) of administration: Oral use Reason for granting waiver: From birth to less than 6 months of age: on the grounds that the specific medicinal product is likely to be unsafe. From 6 months to less than 2 years of age: 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(s):

Treatment of opioid induced constipation (OIC)

2.2 Indication(s) targeted by the PIP:

Treatment of opioid induced constipation (OIC)

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Tablet; Powder for oral suspension

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate powder for oral suspension for oral use.
Non-Clinical Studies	2	Study 2 Dose range-finding juvenile toxicity study. Study 3 Definitive juvenile toxicity study.
Clinical Studies	1	Study 4 (V921F) 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 to less than 18 years of age.
Extrapolation, Modeling & Simulation Studies	2	Study 5 Population pharmacokinetic modelling and simulation study. Study 6 Extrapolation of efficacy of naldemedine from adults to the paediatric population.
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/03/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes