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-100137-PIP01-21-M01

Scope of the Application

Active Substance(s)

linaclotide

Condition(s)

Treatment of functional constipation

Pharmaceutical Form(s)

Capsule, hard

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Allergan Pharmaceuticals International Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Allergan Pharmaceuticals International Limited submitted to the licensing authority on 17/08/2021 07:16 BST an application for a Modification

The procedure started on 02/02/2022 07:51 GMT

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-100137-PIP01-21-M01

Of 17/02/2022 17:35 GMT

On the adopted decision for linaclotide (MHRA-100137-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 linaclotide, Capsule, hard , Oral use .

This decision is addressed to Allergan Pharmaceuticals International Limited, Clonshaugh Business and Technology Park, Dublin, Ireland, D17 E400

ANNEX I

1. Waiver

1.1 Condition:

Treatment of functional constipation The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age Pharmaceutical form(s): Capsule, hard Route(s) of administration: Oral use Reason for granting waiver: on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of functional constipation

2.2 Indication(s) targeted by the PIP:

Treatment of functional constipation

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of capsules for “sprinkles” mode of administration.
Non-Clinical Studies	1	Study 2 A 9-Week Oral Gavage Toxicity Study in Juvenile mice. (MNP-103-054)
Clinical Studies	7	Study 3 Randomised, double-blind, placebo-controlled, dose-ranging study of Linaclotide in children, aged from 6 years to less than 18 years, with Functional Constipation Study 4 Randomised, double-blind, placebo-controlled, ascending-dose, dose-ranging study of Linaclotide in children, aged from 2 years to less than 6 years, with Functional Constipation (LIN-MD-67) Study 5 Randomised, double-blind, placebo-controlled, ascending-dose, dose-ranging study of Linaclotide in children, aged from 6 months to less than 2 years, with Functional Constipation. Study 6 Randomised, double-blind, placebo-controlled, parallel-group, confirmatory study of Linaclotide in children aged from 6 years to less than 18 years with Functional Constipation. (LIN-MD-64) Study 7 Randomised, double-blind, placebo-controlled, parallel-group, confirmatory study of Linaclotide in children aged from 6 months to less than 6 years with Functional Constipation. Study 8 Open label, long-term safety study of Linaclotide in children aged from 6 years to less than 18 years with

		Functional Constipation. (LIN-MD-66) Study 9 Open label, long-term safety study of Linaclotide in children aged from 6 months to less than 6 years with Functional Constipation.
Extrapolation, Modeling & Simulation Studies	0	Not applicable
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:	31/12/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes