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-101044-PIP01-23-M01

Scope of the Application

Active Substance(s)

INCLISIRAN SODIUM

Condition(s)

Treatment of elevated cholesterol

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Novartis Pharmaceuticals UK Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Novartis Pharmaceuticals UK Ltd submitted to the licensing authority on 13/06/2023 12:16 BST an application for a Modification

The procedure started on 23/11/2023 10:47 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-101044-PIP01-23-M01

Of 08/12/2023 16:16 GMT

On the adopted decision for INCLISIRAN SODIUM (MHRA-101044-PIP01-23-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 INCLISIRAN SODIUM, Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Novartis Pharmaceuticals UK Ltd, 2nd Floor, The WestWorks Building White City Place 195 Wood Lane , London , UNITED KINGDOM, W12 7FQ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of elevated cholesterol The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 years of age. Pharmaceutical form(s): Solution for injection Route(s) of administration: SUBCUTANEOUS USE Reason for granting waiver: On the grounds the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of elevated cholesterol.

2.2 Indication(s) targeted by the PIP:

Treatment of heterozygous familial hypercholesterolemia (HeFH). Treatment of homozygous familial hypercholesterolemia (HoFH).

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

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

2.4 Pharmaceutical Form(s):

Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	4	Study 1 (ORION-13; CKJX839C12302) Two-stage, randomised study to evaluate the safety, tolerability and efficacy of inclisiran versus placebo, used in combination with other lipid lowering therapy in paediatric subjects with homozygous familial hypercholesterolaemia (HoFH) from 12 years to less than 18 years of age. Study 2 (ORION-16; CKJX839C12301) Two-stage, randomised study to evaluate the safety, tolerability and efficacy of inclisiran versus placebo, used in combination with other lipid lowering therapy in paediatric patients with heterozygous familial hypercholesterolaemia (HeFH) from 12 years to less than 18 years of age. Study 3 (ORION-19; CKJX839C12304) Two-stage, randomised, controlled versus placebo study to evaluate the safety, tolerability and efficacy of inclisiran, used in combination with other lipid lowering therapy in children with homozygous

		familial hypercholesterolaemia (HoFH) from 6 years to less than 12 years of age. Study 4 (ORION-20; CKJX839C12303) Two-stage, randomised study to evaluate the safety, tolerability and efficacy of inclisiran versus placebo, used in combination with other lipid lowering therapy in paediatric patients with heterozygous familial hypercholesterolaemia (HeFH) from 6 years to less than 12 years of age.
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:	Yes
Date of completion of the paediatric investigation plan:	30/06/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes