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-100248-PIP01-21-M01

Scope of the Application

Active Substance(s)

RISDIPLAM

Condition(s)

Treatment of spinal muscular atrophy

Pharmaceutical Form(s)

Powder for oral solution

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Roche Products Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Roche Products Limited submitted to the licensing authority on 25/10/2021 15:06 BST an application for a Modification

The procedure started on 11/03/2022 16:08 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-100248-PIP01-21-M01

Of 31/03/2022 08:26 BST

On the adopted decision for RISDIPLAM (MHRA-100248-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 RISDIPLAM, Powder for oral solution , Oral use .

This decision is addressed to Roche Products Limited, 6 Falcon Way Shire Park, Welwyn Garden City, United Kingdom, AL71TW

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of spinal muscular atrophy

2.2 Indication(s) targeted by the PIP:

Treatment of spinal muscular atrophy

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

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

2.4 Pharmaceutical Form(s):

Powder for oral solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age appropriate oral liquid dosage form.
Non-Clinical Studies	1	Study 2 In-vitro study in plasma samples of infants, children and adolescents (and adults) to investigate RO7034067 plasma free fraction in the human paediatric population.
Clinical Studies	4	Study 3 Two-part multi-centre study to investigate the efficacy, safety and tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of RO7034067 in patients with type 2 and type 3 SMA (BP39055/ SUNFISH). Study 4 Two-part, multi-centre, single-arm, open-label study to investigate the efficacy, safety and tolerability, pharmacokinetics and pharmacodynamics of RO7034067 in patients with type 1 SMA (BP39056/FIREFISH). Study 5 Multi-centre, exploratory, non-comparative and open-label study to investigate the safety, tolerability, pharmacokinetics and PK/PD relationship of RO7034067 patients with SMA who have previously participated in the Moonfish (BP29420) study with the splicing modifier RO6885247 or previously been treated with nusinersen (SPINRAZA), AVXS-101 or olesoxime (BP39054/JEWELFISH) Study 6 Multi-centre, single-arm, open-label study to investigate the efficacy, safety and tolerability, and PK/PD of RO7034067 in infants genetically diagnosed with SMA and pre-symptomatic (BN40703/ RAINBOWFISH).

Extrapolation, Modeling & Simulation Studies	4	Study 7 Physiologically based pharmacokinetic (PBPK) model of RO7034067 Study 8 Population pharmacokinetic (PopPK) model of RO7034067 Study 9 Extrapolation study to support the use of RO7034067 for the treatment of children with SMA Type 1, 2 and 3 aged between 7 months and 2 years based on extrapolation of in house data from younger infants (Type 1 SMA) and from older children and young adults (Type 2 and 3 SMA) Study 10 Extrapolation study to support the use of RO7034067 for the treatment of ambulant Type 3 SMA patients based on extrapolation of in house data from younger infants (Type 1 SMA) and from older children and young adults (Type 2 and 3 SMA).
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:	30/11/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes