EMA/37955/2023

European Medicines Agency decision

P/0086/2023

of 10 March 2023

on the acceptance of a modification of an agreed paediatric investigation plan for risdiplam (Evrysdi), (EMEA-002070-PIP01-16-M07) 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/0284/2017 issued on 4 October 2017, decision P/0080/2018 issued on 16 March 2018, decision P/0360/2018 issued on 7 December 2018, decision P/0349/2019 issued on 16 September 2019, decision P/0089/2020 issued on 18 March 2020, and decision P/0470/2021 issued on 26 November 2021,

Having regard to the application submitted by Roche Registration GmbH on 18 November 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 20 January 2023, 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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 risdiplam (Evrysdi), powder for oral solution, film-coated tablet, oral use, 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 Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/905358/2022
Amsterdam, 20 January 2023

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

EMEA-002070-PIP01-16-M07

Scope of the application

Active substance(s):

Risdiplam

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of spinal muscular atrophy

Pharmaceutical form(s):

Powder for oral solution

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted to the European Medicines Agency on 18 November 2022 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0284/2017 issued on 4 October 2017, decision P/0080/2018 issued on 16 March 2018, decision P/0360/2018 issued on 7 December 2018, decision P/0349/2019 issued on 16 September 2019, decision P/0089/2020 issued on 18 March 2020, and decision P/0470/2021 issued on 26 November 2021.

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

The procedure started on 3 January 2023.

Scope of the modification

A new pharmaceutical form was added.

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 in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of spinal muscular atrophy

2.1.1. Indication(s) targeted by the PIP

Treatment of spinal muscular atrophy

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for oral solution

Film-coated tablet

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate oral liquid dosage form
Non-clinical studies	**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	**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, modelling and simulation studies	**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	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:	Yes
Date of completion of the paediatric investigation plan:	By November 2023
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 spinal muscular atrophy

Authorised indication(s):

- Treatment of 5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies
  - Invented name(s): Evrysdi
  - Authorised pharmaceutical form(s): Powder for oral solution
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure