EMA/541730/2017

European Medicines Agency decision

P/0284/2017

of 4 October 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral for pyridopyrimidione SMN2 splicing modifier (EMEA-002070-PIP01-16) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Roche Registration Limited on 28 November 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 August 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for pyridopyrimidione SMN2 splicing modifier, powder for oral solution, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for pyridopyrimidione SMN2 splicing modifier, powder for oral solution, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Roche Registration Limited, 6 Falcon Way, Shire Park, AL7 1TW - Welwyn Garden City, United Kingdom.

EMA/PDCO/356356/2017
London, 18 August 2017

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral

EMEA-002070-PIP01-16

Scope of the applications

Active substance(s):

Pyridopyrimidione SMN2 splicing modifier

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 Registration Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Roche Registration Limited submitted for agreement to the European Medicines Agency on 28 November 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 3 January 2017.

Supplementary information was provided by the applicant on 26 May 2017. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

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

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver 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 annex 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.

1.1. Condition:

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

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	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 and children 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. 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. 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 Type 2 and Type 3 SMA who have previously participated in a clinical study with another SMN2-targeting therapy.

		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.
Extrapolation, modelling and 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 PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2020
Deferral for one or more measures contained in the paediatric investigation plan:	Yes