EMA/366137/2020

European Medicines Agency decision

P/0264/2020

of 15 July 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for tominersen (EMEA-002546-PIP01-19) 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 GmbH on 12 July 2019 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 29 May 2020, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 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 and on the granting of a waiver.

(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.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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 tominersen, solution for injection, intrathecal 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 tominersen, solution for injection, intrathecal 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

A waiver for tominersen, solution for injection, intrathecal 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 4

This decision is addressed to Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 – Grenzach, Wyhlen, Germany.

EMA/PDCO/136912/2020
Amsterdam, 29 May 2020

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

EMEA-002546-PIP01-19

Scope of the application

Active substance(s):

Tominersen

Condition(s):

Treatment of Huntington's disease

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intrathecal use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted for agreement to the European Medicines Agency on 12 July 2019 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 20 August 2019.

Supplementary information was provided by the applicant on 21 February 2020. The applicant proposed modifications to the paediatric investigation plan.

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:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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

1.1. Condition:

Treatment of Huntington's disease

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection, intrathecal use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of Huntington's disease

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric Huntington's disease

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of lower strength of solution for injection of tominersen appropriate for the paediatric population from 2 years of age
Non-clinical studies	2	**Study 2** Part 1: First dose range-finding (DRF) juvenile toxicity study in mice to evaluate the feasibility and tolerability of intracerebroventricular injections (ICV) of tominersen and ISIS 444652 (mouse-active surrogate) and to assess brain exposure to these compounds following ICV injection

Area	Number of measures	Description
		Part 2: A second DRF juvenile toxicity study in mice to select the appropriate doses of tominersen and ISIS 444652 for the pivotal juvenile toxicity study **Study 3** Pivotal juvenile toxicity study in mice to evaluate the potential adverse effects during post weaning development following ICV injection of tominersen and ISIS 444652 (mouse active surrogate)
Clinical studies	1	**Study 4** Two part study (Part 1: randomised double-blind sham-controlled and Part 2: open-label active treatment) to evaluate the safety/tolerability, pharmacokinetics and pharmacodynamics of tominersen in children from 2 to less than 18 years of age with Huntington's disease (HD)
Extrapolation, modelling and simulation studies	3	**Study 5** Scaling pre-clinical PK model of tominersen to paediatric population with HD **Study 6** PopPK modelling to characterize PK of tominersen in adult and paediatric patients with HD **Study 7** Part 1: Analysis of existing preclinical, PD and clinical data on tominersen in adults with manifest HD to provide / support efficacy assumptions in the paediatric population based on extrapolation from preclinical models and adults Part 2: Analysis of existing preclinical, PD and clinical data on tominersen in adults with manifest HD and pediatric HD to support the extrapolation approach
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 April 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes