EMA/103545/2014

European Medicines Agency decision

P/0082/2014

of 31 March 2014

on the agreement of a paediatric investigation plan for RNA,[2'-O-(2-methoxyethyl)](P-thio)(m5U-m5C-A- m5C-m5U-m5U-m5U- m5C-A-m5U-A-A-m5U-G- m5C-m5U-G-G) (ISIS 396443) (EMEA-001448-PIP01-13) 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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European Medicines Agency decision

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on the agreement of a paediatric investigation plan for RNA,[2'-O-(2-methoxyethyl)](P-thio)(m5U-m5C-A- m5C-m5U-m5U-m5U- m5C-A-m5U-A-A-m5U-G- m5C-m5U-G-G) (ISIS 396443) (EMEA-001448-PIP01-13) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Isis Pharmaceuticals on 12 April 2013 under Article 16(1) of Regulation (EC) No 1901/2006,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 March 2014, in accordance with Article 18 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, has given an opinion on the agreement of a paediatric investigation plan.

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

[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 RNA,[2'-O-(2-methoxyethyl)](P-thio)(m5U- m5C-A- m5C-m5U-m5U-m5U- m5C-A-m5U-A-A-m5U-G- m5C-m5U-G-G) (ISIS 396443), 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

This decision is addressed to Isis Pharmaceuticals, 2855 Gazelle Ct, 92115 – Carlsbad, United States.

Done at London, 31 March 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/735823/2013

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

EMEA-001448-PIP01-13

Scope of the application

Active substance(s):

RNA,[2'-O-(2-methoxyethyl)](P-thio)(m5U- m5C-A- m5C-m5U-m5U-m5U- m5C-A-m5U-A-A-m5U-G-m5C-m5U-G-G) (ISIS 396443)

Condition(s):

Treatment of spinal muscular atrophy

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intrathecal use

Name/corporate name of the PIP applicant:

Isis Pharmaceuticals

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Isis Pharmaceuticals submitted for agreement to the European Medicines Agency on 12 April 2013 an application for a paediatric investigation plan for the above mentioned medicinal product.

The procedure started on 22 May 2013.

Supplementary information was provided by the applicant on 25 November 2013. The applicant proposed modifications to the paediatric investigation plan.

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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.

   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 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.

London, 14 February 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

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 infantile-onset spinal muscular atrophy;
- Treatment of later-onset 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)

Solution for injection.

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	**Study 1:** Study to determine the local and systemic toxicity of ISIS 396443 following intrathecal lumbar bolus injections to juvenile cynomolgus monkeys for 53 weeks and to assess the reversibility of any effects observed following a 26-week recovery period. **Study 2:** Study to evaluate the pharmacokinetics of ISIS 396443 following multiple dose intrathecal lumbar bolus injections to cynomolgus monkeys.

Clinical studies	4	**Study 3:** Open-label, dose-range finding study to assess the safety and tolerability of multiple doses of ISIS 396443, in children with spinal muscular atrophy from 2 to less than 15 years of age. **Study 4:** Open-label, dose-range finding study to assess the safety and tolerability of multiple doses of ISIS 396443, in neonates and infants with spinal muscular atrophy from 21 days to less than 8 months. **Study 5:** Double-blind, randomised, sham-procedure controlled study to assess the safety and efficacy of ISIS 396443 as compared to sham-injection, in neonates and infants from birth to less than or equal to 6 months of age at screening or ≤ 8 months of age at screening with symptom onset within 120 days of age at screening. **Study 6:** Double-blind, randomised, sham-procedure controlled study to assess the safety and efficacy of ISIS 396443 as compared to sham-injection, in children with spinal muscular atrophy from 6months to less than 18 years of age.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2016
Deferral for one or more measures contained in the paediatric investigation plan:	No