EMA/631879/2019

European Medicines Agency decision

P/0426/2019

of 6 December 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues (DCR-PHXC) (EMEA-002493-PIP01-18) 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 Dicerna EU Limited on 25 November 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 October 2019, in accordance with Article 17 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 synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues (DCR-PHXC), solution for injection/infusion, subcutaneous use, intravenous 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 synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues (DCR-PHXC), solution for injection/infusion, subcutaneous use, intravenous 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 Dicerna EU Limited, 3rd Floor, 11-12 St James's Square, SW1Y 4LB - London, United Kingdom.

EMA/PDCO/410628/2019
Amsterdam, 18 October 2019

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

EMEA-002493-PIP01-18

Scope of the application

Active substance(s):

Synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues (DCR-PHXC)

Condition(s):

Treatment of primary hyperoxaluria

Pharmaceutical form(s):

Solution for injection/infusion

Route(s) of administration:

Subcutaneous use

Intravenous use

Name/corporate name of the PIP applicant:

Dicerna EU Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Dicerna EU Limited submitted for agreement to the European Medicines Agency on 25 November 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 3 January 2019.

Supplementary information was provided by the applicant on 15 July 2019. 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 report:

   - 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.

   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.

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 primary hyperoxaluria

2.1.1. Indication(s) targeted by the PIP

Treatment of primary hyperoxaluria

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/infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Development of an age-appropriate solution for subcutaneous injection
Non-clinical studies	0	Not applicable
Clinical studies	6	**Study 2 (DCR-PHXC-101):** Open-label, single-arm trial to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of single ascending doses of DCR-PHXC in paediatric subjects from 12 to less than 18 years of age with primary hyperoxaluria type 1 (PH1) or 2 (PH2) and healthy adult volunteers. **Study 3 (DCR-PHXC-301):** Open-label, long-term rollover study to evaluate efficacy and safety of DCR-PHXC in paediatric subjects from 6 to less than 18 years of age (and adults) with primary hyperoxaluria type 1 (PH1), 2 (PH2) or 3 (PH3). **Study 4 (DCR-PHXC-201):** Double-blind, randomised, placebo-controlled trial to evaluate efficacy, safety and pharmacokinetics of DCR-PHXC in paediatric subjects from 6 to less than 18 years of age (and adults) with primary hyperoxaluria type 1 (PH1) or 2 (PH2) and relatively intact renal function.

		Study 5 (DCR-PHXC-104): Open-label, single-arm proof of concept trial to evaluate pharmacokinetics, pharmacodynamics and safety of DCR-PHXC in paediatric patients from 6 to less than 18 years of age (and adults) with primary hyperoxaluria type 3 (PH3). **Study 6 (DCR-PHXC-203):** Open-label, single-arm trial to evaluate pharmacokinetics, safety and efficacy of DCR-PHXC in paediatric patients from birth to less than 6 years of age with primary hyperoxaluria type 1 (PH1), 2 (PH2) or 3 (PH3) and relatively intact renal function. **Study 7 (DCR-PHXC-204):** Open-label, single-arm trial to evaluate pharmacokinetics, safety and efficacy of DCR-PHXC in paediatric patients from birth to less than 18 years of age with primary hyperoxaluria type 1 (PH1) or 2 (PH2) and impaired renal function.
Extrapolation, modelling and simulation studies	3	**Study 8 (DIC201804; intact renal function):** Modelling and simulation study to support dose finding of DCR-PHXC in children from 6 to less than 18 years with primary hyperoxaluria and relatively intact renal function. **Study 9:** Modelling and simulation study to evaluate the use of DCR-PHXC in children from 6 to less than 18 years with primary hyperoxaluria and impaired renal function. **Study 10:** Modelling and simulation study to evaluate the use of DCR-PHXC in children from birth to less than 6 years of age with primary hyperoxaluria and relatively intact renal function (follow-up to Study 8).
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:	No
Date of completion of the paediatric investigation plan:	By January 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes