EMA/71430/2021

European Medicines Agency decision

P/0071/2021

of 17 March 2021

on the acceptance of a modification of an agreed 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) (EMEA-002493-PIP01-18-M02) 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 European Medicines Agency's decision P/0426/2019 issued on 6 December 2019 and the decision P/0342/2020 issued on 9 September 2020,

Having regard to the application submitted by Dicerna Ireland Limited on 26 October 2020 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 29 January 2021, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed 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, subcutaneous 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 Dicerna Ireland Limited, Mespil House, Sussex Road, D04 T4A6 – Dublin, Ireland.

EMA/PDCO/589228/2020
Amsterdam, 29 January 2021

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

EMEA-002493-PIP01-18-M02

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

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Dicerna Ireland Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Dicerna Ireland Limited submitted to the European Medicines Agency on 26 October 2020 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0426/2019 issued on 6 December 2019 and the decision P/0342/2020 issued on 9 September 2020.

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

The procedure started on 1 December 2020.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

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 Norwegian Paediatric Committee member 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 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

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	7	**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):** Double-blind, randomised, placebo-controlled study to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics 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 with or without dialysis. **Study 11 (DCR-PHXC-502)** *This study was added as a result of procedure EMEA-002493-PIP01-18-M02.* Non-interventional, natural history study to collect data on the rate of new stone formation and the degree of nephrocalcinosis in patients from birth to less than 18 years of age (and adults) with primary hyperoxaluria type 3 (PH3) and relatively intact renal function
Extrapolation, modelling and simulation studies	3	**Study 8 (DIC201804):** Modelling and simulation study to support dose finding of DCR-PHXC in children from 6 to less than 18 years of age with primary hyperoxaluria and relatively intact renal function. **Study 9:** Modelling and simulation study to evaluate the use of DCR-PHXC in children from birth to less than 18 years of age 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 December 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes