EMA/591389/2024

European Medicines Agency decision

P/0402/2024

of 18 December 2024

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for diazoxide choline, (EMEA-003614-PIP01-24) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Soleno Therapeutics Europe Ltd. on 22 March 2024 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 13 December 2024, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for diazoxide choline, prolonged-release tablet, age-appropriate oral dosage form, 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 diazoxide choline, prolonged-release tablet, age-appropriate oral dosage form, 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

A waiver for diazoxide choline, prolonged-release tablet, age-appropriate oral dosage form, 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 4

This decision is addressed to Soleno Therapeutics Europe Ltd., Suite 10151, 26 Upper Pembroke Street, Dublin 2 - Dublin, Ireland.

EMA/PDCO/442063/2024
Amsterdam, 13 December 2024

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

EMEA-003614-PIP01-24

Scope of the application

Active substance(s):

Diazoxide choline

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of Prader-Willi syndrome

Pharmaceutical form(s):

Prolonged-release tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Soleno Therapeutics Europe Ltd.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Soleno Therapeutics Europe Ltd. submitted for agreement to the European Medicines Agency on 22 March 2024 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 29 April 2024.

Supplementary information was provided by the applicant on 6 September 2024. 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;
   - 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 Paediatric Committee members of Liechtenstein and Norway agree 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 annexes 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 Prader-Willi syndrome

The waiver applies to:

- the paediatric population from birth to less than 4 years of age;
- prolonged-release tablet, age-appropriate oral dosage form, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Treatment of Prader-Willi syndrome

2.1.1. Indication(s) targeted by the PIP

Chronic treatment of hyperphagia in patients aged over 4 years with Prader-Willi syndrome (PWS)

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

From 4 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Prolonged-release tablet

Age-appropriate oral dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate formulation
Non-clinical studies	Not applicable
Clinical studies	**Study 2 (PC025)** Randomised withdrawal study of diazoxide choline (DCCR) extended-release tablets, to evaluate safety of multiple dose levels in patients aged from 10 years to less than 18 years of age (and adults up to 22 years of age) with Prader-Willi syndrome with an open-label extension.

	Study 3 (C601) Randomised, double-blind, placebo-controlled, parallel-arm, phase 3 study comparing the effects of DCCR in patients aged from 4 years to less than 18 years of age with genetically-confirmed Prader-Willi syndrome with hyperphagia. **Study 4 (C602-OLE)** Open-label study to evaluate the long-term safety and efficacy of DCCR to treat Prader-Willi syndrome in participants aged from 4 years to less than 18 years of age who completed clinical Study C601. **Study 5 (C602-RWP)** Double-blind, placebo-controlled, randomised withdrawal period to evaluate the effects of discontinuation of treatment with DCCR and the initiation of placebo compared with continued treatment with DCCR in patients aged from 4 years to less than 18 years of age who were taking DCCR in study C601. **Study 6 (C614)** Open-label, multicentre, study to evaluate long-term safety and effectiveness of DCCR in patients aged from 4 years to less than 18 years of age with genetically-confirmed Prader-Willi syndrome. **Study 7** Preliminary efficacy and safety clinical study in the paediatric population with Prader-Willi syndrome.
Modelling and simulation analyses	**Study 8 (SOLE-PMX-DCCR-2095)** DCCR Exposure-response modelling of Clinical Study C601 Results in patients with a genetically confirmed diagnosis of Prader-Willi syndrome aged from 4 years to less than 18 years of age with hyperphagia. **Study 9 (DCCR-PMX-003/ RPT-CL-011)** Population pharmacokinetic analysis of DCCR in adult participants with Prader-Willi syndrome and non- Prader-Willi syndrome. **Study 10 (DCCR-PMX-004/ RPT-CL-002)** Exposure-response analysis of DCCR in paediatric participants from 4 years to less than 18 years of age with Prader-Willi syndrome and adult participants with or without Prader-Willi syndrome. **Study 11 (DCCR-PMX-006/ RPT-CL-016)** Population pharmacokinetic analysis of DCCR and longitudinal exposure-efficacy analysis of Hyperphagia Questionnaire for Clinical Trials (HQ-CT) in paediatric participants from 4 years to less than 18

	years of age with Prader-Willi syndrome and adult participants with or without Prader-Willi syndrome.
Other studies	Not applicable
Extrapolation plan	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 2032
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.