



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMADOC-1700519818-2035722

European Medicines Agency decision

EMA/PE/0000229606

of 14 April 2025

on the acceptance of a modification of an agreed paediatric investigation plan for alanine, arginine, aspartic acid, calcium chloride dihydrate, deferoxamine mesilate, glycine, histidine, L-tryptophan, magnesium chloride hexahydrate, N-acetylhistidine monohydrate, N-hydroxy-3,4-dimethoxy-N-methyl-benzamide, oxogluric acid, potassium chloride, sodium chloride 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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/0228/2021 issued on 9 June 2021 and the decision P/0210/2023 issued on 14 June 2023,

Having regard to the application submitted by Dr. Franz Koehler Chemie GmbH on 23 November 2024 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 28 February 2025, 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 and to the deferral.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan including changes to the deferral.

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

Changes to the agreed paediatric investigation plan for alanine, arginine, aspartic acid, calcium chloride dihydrate, deferoxamine mesilate, glycine, histidine, L-tryptophan, magnesium chloride hexahydrate, N-acetylhistidine monohydrate, N-hydroxy-3,4-dimethoxy-N-methyl-benzamide, oxogluric acid, potassium chloride, sodium chloride, including changes to the deferral, 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 Dr. Franz Koehler Chemie GmbH, Werner-Von-Siemens-Strasse 14-28, 64625 Bensheim, Germany.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMADOC-1700519818-1809214
Amsterdam, 28 February 2025

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA/PE/0000229606

Scope of the application

Active substance(s):

Alanine, arginine, aspartic acid, calcium chloride dihydrate, deferoxamine mesilate, glycine, histidine, L-tryptophan, magnesium chloride hexahydrate, N-acetylhistidine monohydrate, N-hydroxy-3,4-dimethoxy-N-methyl-benzamide, oxogluric acid, potassium chloride, sodium chloride

Invented name and authorisation status:

See Annex II

Condition(s):

Cardioplegia

Pharmaceutical form(s):

Concentrate and solvent for solution for infusion

Route(s) of administration:

Intracoronary use

Name/corporate name of the PIP applicant:

Dr. Franz Köhler Chemie GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Dr. Franz Köhler Chemie GmbH submitted to the European Medicines Agency on 21 November 2024 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0228/2021 issued on 9 June 2021 and the decision P/0210/2023 issued on 14 June 2023.

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

The procedure started on 2 January 2025.



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 and to the deferral in the scope set out in the Annex I of this opinion.

The Paediatric Committee member of Norway 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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Cardioplegia

2.1.1. Indication(s) targeted by the PIP

For induction of cardioplegia in paediatric patients of all ages undergoing cardiac surgery to correct congenital heart malformation in operations requiring cardiopulmonary bypass support.

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)

Concentrate and solvent for solution for infusion

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	<p>Study 1 (FKC-001_02_rat_tox_iv)</p> <p>Single dose intravenous toxicity study of 3,4-dimethoxy-N-methylbenzohydroxamic acid in rats.</p> <p><i>This study is identical with Study 1 in EMEA-002735-PIP03-20 for the condition: Heart transplantation.</i></p> <p>Study 2 (FKC-003_01_dev_reprotox Rat)</p> <p>Reproductive toxicity study of 3,4-dimethoxy-N-methylbenzohydroxamic acid in rats.</p> <p><i>This study is identical with Study 1 in EMEA-002735-PIP03-20 for the condition: Heart transplantation.</i></p>
Clinical studies	<p>Study 3 (CL-N-HTX-Paed-II/10/20)</p> <p>Randomised single-blind study to investigate the safety and the cardioprotective effects of custodiol-N to those of its precursor product in children from birth to less than 18 years of age undergoing heart surgery with cardiopulmonary bypass</p>

Extrapolation, modelling and simulation studies	Not applicable
Other studies	Not applicable
Other measures	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 July 2027
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.