EMA/330466/2023

European Medicines Agency decision

P/0324/2023

of 11 August 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver for encaleret (EMEA-003348-PIP01-22) 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 Calcilytix Therapeutics, Inc. a BridgeBio Company on 17 October 2022 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 23 June 2023, 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 refusal 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 refusing 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 encaleret, film-coated 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 encaleret, film-coated 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 encaleret, film-coated 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 refused.

Article 4

This decision is addressed to Calcilytix Therapeutics, Inc a BridgeBio Company, 1800 Owens Street, Suite C-1200, 94158 - San Francisco, California United States.

EMA/PDCO/141104/2023 Corr[1]
Amsterdam, 23 June 2023

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

EMEA-003348-PIP01-22

Scope of the application

Active substance(s):

Encaleret

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of hypoparathyroidism

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Calcilytix Therapeutics, Inc. a BridgeBio Company

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Calcilytix Therapeutics, Inc. a BridgeBio Company submitted for agreement to the European Medicines Agency on 17 October 2022 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 21 November 2022.

[1] 20 July 2023

Supplementary information was provided by the applicant on 20 March 2023. 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 refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population and the above mentioned condition(s) as it does not meet the grounds detailed in Article 11(1) of said Regulation.

   The Paediatric Committee member of Norway 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 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 hypoparathyroidism

The request for the waiver applied to:

- the paediatric population from birth to less than 6 months of age;
- film-coated tablet, age-appropriate oral dosage form, oral use;

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (a) the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;
- (b) the disease or condition for which the specific medicinal product is intended occurs only in adult populations;
- (c) the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Because:

- the PDCO disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe;
- the disease or condition for which the specific medicinal product is intended, does occur in the paediatric population(s);
- measures would be justified by the expected therapeutic benefit and clinical trials may be feasible;
- the specific medicinal product may represent a significant therapeutic benefit as the needs are not met;
- clinical studies may fulfil a therapeutic need of the paediatric population.

The waiver request is therefore refused by the PDCO.

2. Paediatric investigation plan

2.1. Condition:

Treatment of hypoparathyroidism

2.1.1. Indication(s) targeted by the PIP

Treatment of autosomal dominant hypocalcaemia type 1 (ADH1)

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)

Film-coated tablet

Age-appropriate oral dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate oral dosage form suitable for children from birth to less than 6 years of age
Non-clinical studies	**Study 2 (CLTX-TX-032)** Dose range-finding juvenile toxicity study to assess toxicokinetics of encaleret in juvenile Sprague-Dawley rats **Study 3 (CLTX-TX-033)** Definitive juvenile toxicity study of encaleret in juvenile Sprague-Dawley rats, including clinical pathology and toxicokinetic evaluation, bone (femur) growth measurements, ex vivo bone densitometry and microscopic sperm evaluation / staging
Clinical studies	**Study 4 (CLTX-305-303)** Open-label, historical-controlled trial to evaluate pharmacokinetics, safety and efficacy of encaleret in children from birth to less than 18 years of age with autosomal dominant hypocalcaemia Type 1 (ADH1)
Modelling and simulation studies	**Study 5** Modelling and simulation study to evaluate the use of encaleret in children from birth to less than 18 years of age with autosomal dominant hypocalcaemia Type 1 (ADH1)
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:	Yes
Date of completion of the paediatric investigation plan:	By December 2026
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.