EMADOC-1700519818-2117339

European Medicines Agency decision

EMA/PE/0000232780

Of 15 May 2025

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for probenecid 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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on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for probenecid in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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

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

Having regard to the application submitted by PannTheraPi on 31 May 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 28 March 2025, 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.

Has adopted this decision:

Article 1

A paediatric investigation plan for probenecid, 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 probenecid, 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 probenecid, 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 PannTheraPi, 10 Rue Descartes, 30000 - Nimes, France.

EMADOC-1700519818-1861254
Amsterdam, 28 March 2025

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

EMA/PE/0000232780

Scope of the application

Active substance(s):

Probenecid

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of seizures associated with focal cortical dysplasia

Pharmaceutical form(s):

Prolonged-release granules

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

PannTheraPi

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, PannTheraPi submitted for agreement to the European Medicines Agency on 31 may 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 27 January 2025.

Supplementary information was provided by the applicant on 17 December 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 member of Norway agrees 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 seizures associated with focal cortical dysplasia

The waiver applies to:

- neonates from birth to less than 28 days of age;
- plonged-release granules, oral use, gastric use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of seizures associated with focal cortical dysplasia

2.1.1. Indication(s) targeted by the PIP

Treatment of seizures associated with focal cortical dysplasia (FCD)

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

From 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Prolonged-release granules

2.1.4. Measures

Area	Description
Quality-related studies	Study 1 Development of an appropriate dispensing device for prolonged-release granules. Generation of data on acceptability and palatability during the clinical trial(s) with the target population. Assessment of suitability for administration via a feeding tube, and in combination with common foods and drinks.
Non-clinical studies	Study 2 Definitive juvenile toxicity study
Clinical studies	Study 3 Double-blind, randomised, multiple-dose, placebo-controlled trial to evaluate pharmacokinetics (PK), safety, efficacy, acceptability/palatability of probenecid as add-on

	to best standard of care in children from 2 years to less than 18 years of age with seizures associated with focal cortical dysplasia (FCD). Study 4 Open-label, multiple-dose, single-arm trial to evaluate pharmacokinetics, safety, activity, acceptability/palatability of probenecid as add-on to best standard of care in children from 28 days to less than 2 years of age with seizures associated with focal cortical dysplasia (FCD).
Modelling and simulation analyses	Study 5 Development of a population pharmacokinetic/pharmacodynamic (PopPK/PD) model to predict paediatric doses for use in Study 3, to be further refined in Study 7 to support extrapolation of efficacy from adults and older children to children from 28 days to less than 2 years of age. Study 6 Development of a physiologically-based pharmacokinetic/pharmacodynamic (PBPK/PD) model to further inform paediatric dosing in Studies 3 and 4. Study 7 Development of a population-based pharmacokinetic/pharmacodynamic (PopPK/PD) model to predict paediatric doses for the use in Study 4 and to support extrapolation of efficacy from adults and older children to children from 28 days to less than 2 years of age.
Other studies	Not applicable
Extrapolation plan	Studies 3, 4, 5, 6, 7 are part of an extrapolation plan covering the paediatric population from 28 days to less than 18 years of age, as agreed by the PDCO.

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 2036
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.