EMA/400670/2023

European Medicines Agency decision

P/0398/2023

of 27 October 2023

on the acceptance of a modification of an agreed paediatric investigation plan for brivaracetam (Briviact), (EMEA-000332-PIP02-17-M05) 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 European Medicines Agency's decision P/0052/2018 issued on 22 February 2018, the decision P/0203/2020 issued on 12 June 2020, the decision P/0173/2021 issued on 9 April 2021, the decision P/0003/2022 issued on 18 January 2022, and the decision P/0093/2023 issued on 10 March 2023,

Having regard to the application submitted by UCB Pharma S.A. on 23 June 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 8 September 2023, 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 brivaracetam (Briviact), film-coated tablet, oral solution, solution for injection/infusion, oral use, intravenous use, 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/126/2009 issued on 13 July 2009, including subsequent modifications thereof.

Article 3

This decision is addressed to UCB Pharma S.A., Allée de la Recherche 60, 1070 - Brussels, Belgium.

EMA/PDCO/322746/2023
Amsterdam, 8 September 2023

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

EMEA-000332-PIP02-17-M05

Scope of the application

Active substance(s):

Brivaracetam

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of paediatric epilepsy syndromes

Treatment of neonatal seizures

Pharmaceutical form(s):

Film-coated tablet

Oral solution

Solution for injection/infusion

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

UCB Pharma S.A.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, UCB Pharma S.A. submitted to the European Medicines Agency on 23 June 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0052/2018 issued on 22 February 2018, the decision P/0203/2020 issued on 12 June 2020, the decision P/0173/2021 issued on 9 April 2021, the decision P/0003/2022 issued on 18 January 2022, and the decision P/0093/2023 issued on 10 March 2023.

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

The procedure started on 14 August 2023.

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 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 paediatric epilepsy syndromes

The waiver applies to:

- preterm newborn infants, term newborn infants (from birth to less than 28 days of age);
- film-coated tablet, oral solution, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

1.2. Condition

Treatment of neonatal seizures

The waiver applies to:

- the paediatric population from 28 days to less than 18 years of age;
- film-coated tablet, oral solution, solution for injection, oral use, intravenous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan

2.1. Condition

Treatment of paediatric epilepsy syndromes

2.1.1. Indication(s) targeted by the PIP

Treatment of refractory paediatric epilepsy syndromes

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)

Film-coated tablet

Oral solution

2.1.4. Measures

Area	Description
Quality	Not applicable
Non-clinical	**Study 1 (NCD1671)** 9-week oral toxicity study followed by a 30-day recovery period in juvenile rats. *(same study as in EMEA-000332-PIP01-08-M13)* **Study 2 (NCD1883)** Study to evaluate brain weight in juvenile and adult rats. *(same study as in EMEA-000332-PIP01-08-M13)* **Study 3 (NCD1863)** 9-month oral toxicity study in juvenile dogs with a 2-months recovery period. *(same study as in EMEA-000332-PIP01-08-M13)*
Clinical	**Study 4 (N01313)** In silico study for prediction of brivaracetam disposition in children. (same study as in EMEA-000332-PIP01-08-M13) **Study 5 (N01263)** Open-label, single-arm, multi-centre, pharmacokinetic, safety and efficacy study of adjunctive administration of brivaracetam in children aged 1 month to less than 16 years with refractory paediatric epilepsy syndromes or epilepsy. *(same study as in EMEA-000332-PIP01-08-M13)* **Study 6 (N01269)** Randomized, dose-finding and confirmatory, double-blind, placebo-controlled, parallel-group, multicentre study with a 2-stage adaptive design and randomized withdrawal to evaluate the efficacy, safety, and tolerability of brivaracetam as monotherapy **Study 7** *deleted as part of EMEA-000332-PIP02-17-M02* **Study 10 (EP0132)** *added as part of part of EMEA-000332-PIP02-17-M02* Open-label, single-arm, multi-centre, long-term follow-up study to evaluate long-term safety, tolerability, and efficacy of brivaracetam.

2.2. Condition

Treatment of neonatal seizures

2.2.1. Indication(s) targeted by the PIP

Treatment of neonatal seizures with adjunctive administration of brivaracetam

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

From birth to less than 28 days

2.2.3. Pharmaceutical form(s)

Solution for injection

Oral solution

2.2.4. Measures

Area	Description
Quality	Not applicable
Non-clinical	**Study 1 (NCD1671)** Same as study 1 for condition of treatment of paediatric epilepsy syndromes. **Study 2 (NCD1883)** Same as study 2 for condition of treatment of paediatric epilepsy syndromes. **Study 3 (NCD1863)** Same as study 3 for condition of treatment of paediatric epilepsy syndromes.
Clinical	**Study 4 (N01313)** Same as study 4 for condition of treatment of paediatric epilepsy syndromes. **Study 8 (N01331)** Modelling and simulation of intravenous brivaracetam pharmacokinetic profiles in children to evaluate dose adaptation rules. **Study 9 (N01349)** *modified as part of EMEA-000332-PIP02-17-M03* Open-label study to evaluate safety, pharmacokinetics and activity of brivaracetam in neonates with repeated electroencephalographic seizures assessed by video-EEG.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2025
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:

Condition(s) and authorised indication(s)

1. Treatment of partial-onset seizures

Authorised indication(s):

- Briviact is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with epilepsy
  - Invented name(s): Briviact
  - Authorised pharmaceutical form(s): Film-coated tablet, oral solution, solution for injection/infusion
  - Authorised route(s) of administration: Oral use, intravenous use
  - Authorised via centralised procedure