EMA/198014/2021

European Medicines Agency decision

P/0173/2021

of 9 April 2021

on the acceptance of a modification of an agreed paediatric investigation plan for brivaracetam (Briviact), (EMEA-000332-PIP02-17-M02) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary 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, and decision P/0203/2020 issued on 12 June 2020,

Having regard to the application submitted by UCB Pharma S.A. on 17 December 2020 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 26 March 2021, 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 and to the waiver.

(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 and to the waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for brivaracetam (Briviact), film-coated tablet, oral solution, solution for injection, oral use, intravenous use, including changes to the deferral and to the waiver, 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/0052/2018 issued on 22 February 2018 including subsequent modifications thereof.

Article 3

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

EMA/PDCO/65494/2021 Corr
Amsterdam, 26 March 2021

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

EMEA-000332-PIP02-17-M02

Scope of the application

Active substance(s):

Brivaracetam

Invented name:

Briviact

Condition(s):

Treatment of paediatric epilepsy syndromes

Treatment of neonatal seizures

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Oral solution

Solution for injection

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

UCB Pharma S.A.

Information about the authorised medicinal product:

See Annex II

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 17 December 2020 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, and decision P/0203/2020 issued on 12 June 2020.

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

The procedure started on 26 January 2021.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Amendment of the scope of the Paediatric Investigation Plan to include another condition.

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

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);
- film-coated tablet and 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 and solution for injection, oral use and 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

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Oral solution

2.1.4. Measures

Area	Number of studies	Description
Quality	0	Not applicable

Non-clinical	3	**Study 1** 9-week oral toxicity study followed by a 30-day recovery period in juvenile rats. (NCD1671, same study as in EMEA-000332-PIP01-08-M13) **Study 2** Study to evaluate brain weight in juvenile and adult rats. (NCD1883, same study as in EMEA-000332-PIP01-08-M13) **Study 3** 9-month oral toxicity study in juvenile dogs with a 2-months recovery period. (NCD1863, same study as in EMEA-000332-PIP01-08-M13)
Clinical	4	**Study 4** In silico study for prediction of brivaracetam disposition in children. (N01313, same study as in EMEA-000332-PIP01-08-M13) **Study 5** 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. (N01263, same study as in EMEA-000332-PIP01-08-M13) **Study 6** 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 (N01269) **Study 7 – deleted as part of EMEA-000332-PIP02-17-M02** **Study 10 – 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 (EP0132).

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

2.2.4. Measures

Area	Number of studies	Description
Quality	0	Not applicable
Non-clinical	3	**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	3	**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)** 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 January 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

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

Authorised pharmaceutical form(s):

Film-coated tablet

Oral solution

Solution for injection/infusion

Authorised route(s) of administration:

Oral use

Intravenous use