EMA/416812/2020

European Medicines Agency decision

P/0324/2020

of 12 August 2020

on the acceptance of a modification of an agreed paediatric investigation plan for brivaracetam (Briviact and associated names) (EMEA-000332-PIP01-08-M15) 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/126/2009 issued on 13 July 2009, the decision P/37/2010 issued on 31 March 2010, the decision P/195/2010 issued on 26 October 2010, the decision P/49/2011 issued on 4 March 2011, the decision P/211/2011 issued on 2 September 2011, the decision P/0016/2012 issued on 25 January 2012, the decision P/0078/2013 issued on 27 March 2013, the decision P/0305/2013 issued on 28 November 2013, the decision P/0127/2014 issued on 22 May 2014, the decision P/0242/2015 issued on 30 October 2015, the decision P/0182/2016 issued on 15 July 2016, the decision P/0048/2017 issued on 23 February 2017, the decision P/0240/2017 issued on 11 August 2017, the decision P/0051/2018 issued on 22 February 2018 and the decision P/0297/2019 issued on 12 August 2019,

Having regard to the application submitted by UCB Pharma S.A. on 10 June 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 24 July 2020, 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.
[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 and associated names), film-coated tablet, oral solution, solution for injection, 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 is addressed to UCB Pharma S.A., Allee de la Recherche, 60, 1070 – Brussels, Belgium.

EMA/PDCO/317913/2020
Amsterdam, 24 July 2020

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

EMEA-000332-PIP01-08-M15

Scope of the application

Active substance(s):

Brivaracetam

Invented name:

Briviact and associated names

Condition(s):

Treatment of neonatal seizures

Treatment of epilepsy with partial onset 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 10 June 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/126/2009 issued on 13 July 2009, the decision P/37/2010 issued on 31 March 2010, the decision P/195/2010 issued on 26 October 2010, the decision P/49/2011 issued on 4 March 2011, the decision P/211/2011 issued on 2 September 2011, the decision P/0016/2012 issued on 25 January 2012, the decision P/0078/2013 issued on 27 March 2013, the decision P/0305/2013 issued on 28 November 2013, the decision P/0127/2014 issued on 22 May 2014, the decision P/0242/2015 issued on 30 October 2015, the decision P/0182/2016 issued on 15 July 2016, the decision P/0048/2017 issued on 23 February 2017, the decision P/0240/2017 issued on 11 August 2017, the decision P/0051/2018 issued on 22 February 2018 and the decision P/0297/2019 issued on 12 August 2019.

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

The procedure started on 6 July 2020.

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 Norwegian Paediatric Committee member 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 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 neonatal seizures

2.1.1. Indication(s) targeted by the PIP

Treatment of neonatal seizures with adjunctive administration of brivaracetam

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

From birth to less than 28 days

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Number of studies	Description
Quality	0	Not applicable
Non-clinical	3	**Study 1 (NCD1671)** 9-week oral toxicity study followed by a 30-day recovery period in juvenile rats *(same study as in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes")* **Study 2 (NCD1883)** Study to evaluate brain weight in juvenile and adult rats *(same study as in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes")*

		Study 3 (NCD1863) 9-month oral toxicity study in juvenile dogs with a 2-months recovery period *(same study as in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes")*
Clinical	4	**Study 4 (N01313)** In silico study for prediction of brivaracetam disposition in children *(same study as in EMEA-000332-PIP02-17 for condition "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. **Study 7 (N01266)** Open-label, single-arm, long-term follow-up study of brivaracetam in children with epilepsy *(same study as in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes")*

2.2. Condition

Treatment of epilepsy with partial onset seizures

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with partial onset seizures

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Oral solution

Solution for injection

2.2.4. Measures

Area	Number of studies	Description
Quality	0	Not applicable
Non-clinical	3	**Study 1 (NCD1671)** *The same study as for "Treatment of neonatal seizures" and in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes"* **Study 2 (NCD1883)** *The same study as for "Treatment of neonatal seizures" and in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes"* **Study 3 (NCD1863)** *The same study as for "Treatment of neonatal seizures" and in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes"*
Clinical	4	**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 of age with refractory paediatric epilepsy syndromes or epilepsy *(same study as in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes")* **Study 7 (N01266)** *The same study as for "Treatment of neonatal seizures" and in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes"* **Study 9 (N01349)** *The same study as for "Treatment of neonatal seizures" and in EMEA-000332-PIP02-17 for condition "Treatment of Paediatric Epilepsy Syndromes"* **Study 10** Systematic review of the literature of all published trials focusing on the possibility of extrapolating efficacy from adult to paediatric patients with partial onset seizures.

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 July 2022
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 epilepsy with 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 adults, adolescents and children from 4 years of age with epilepsy.

Authorised pharmaceutical form(s):

Film-coated tablets

Oral solution

Solution for injection

Authorised route(s) of administration:

Oral use

Intravenous use