EMA/36974/2012

European Medicines Agency decision

P/0016/2012

of 25 January 2012

on the acceptance of a modification of an agreed paediatric investigation plan for brivaracetam (EMEA-000332-PIP01-08-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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on the acceptance of a modification of an agreed paediatric investigation plan for brivaracetam (EMEA-000332-PIP01-08-M05) 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[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 and the decision P/211/2011 issued on 2 September 2011,

Having regard to the application submitted by UCB Pharma SA on 3 October 2011 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 9 December 2011, 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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, film-coated tablet, oral solution, solution for injection, oral use, intravenous use 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 SA, 60 Allée de la Recherche, 1070 - Bruxelles, Belgium.

Done at London, 25 January 2012

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/36974/2012

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

EMEA-000332-PIP01-08-M05

Scope of the application

Active substance(s):

Brivaracetam

Condition(s):

Treatment of paediatric epilepsy syndromes

Treatment of neonatal seizures

Treatment of epilepsy with partial onset seizures

Treatment of generalised epilepsy

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 SA

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, UCB Pharma SA submitted to the European Medicines Agency on 3 October 2011 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

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P/195/2010 issued on 26 October 2010, the decision P/49/2011 issued on 4 March 2011 and P/211/2011 issued on 2 September 2011.

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

The procedure started on 12 October 2011.

Scope of the modification

Some measures of the original opinion 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 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 annex(es) and appendix.

London, 9 December 2011

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

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

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);
- for 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).

1.2. Condition: Treatment of neonatal seizures

The waiver applies to:

- Infants and toddlers (from 28 days to less than 24 months), Children (from 2 to less than 12 years), Adolescents (from 12 to less than 18 years);
- for 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).

1.3. Condition: Treatment of generalised epilepsy

The waiver applies to:

- Preterm newborn infants, Term newborn infants (from birth to less than 28 days);
- for 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 with adjunctive administration of brivaracetam.

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

From 1 month to less than 18 years.

2.1.3. Pharmaceutical form(s)

Film-coated tablet (10 mg, 25 mg and 50 mg), oral solution (1 mg/ml, 10 mg/ml) for oral use.

2.1.4. Studies

Area	**Number of studies**	**Description**
Quality	-	Not applicable.
Non-clinical	3	**Study 1** 9-week oral toxicity study followed by a 30-day recovery period in juvenile rats. **Study 2** Study to evaluate brain weight in juvenile and adult rats. **Study 3** 9-month oral toxicity study in juvenile dogs with a 2-months recovery period.
Clinical	4	**Study 4** In silico study for prediction of brivaracetam disposition in children. **Study 5** Open-label, single-arm, multi-center, 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. **Study 6** Randomized, double-blind, placebo-controlled, parallel-group, multicentre study to evaluate the efficacy, safety, and tolerability of brivaracetam as adjunctive therapy in patients aged 1 month to 16 years with a paediatric epileptic syndrome based on the results of the

		open label observational study. **Study 7** Open-label, single-arm, long-term follow-up study in children with epilepsy.

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, intravenous use.

2.2.4. Studies

Area	Number of studies	Description
Quality	-	Not applicable.
Non-clinical	3	Same as for condition "Treatment of Paediatric Epilepsy Syndromes "
Clinical	4	**Study 4** In silico study for prediction of brivaracetam disposition in children. **Study 8** Modelling and simulation of intravenous brivaracetam pharmacokinetic profiles in children to evaluate dose adaptation rules. **Study 9** Open, randomised, parallel group, active controlled study to evaluate efficacy, safety and pharmacokinetics in neonates with repeated seizures. **Study 7** Open-label, single-arm, long-term follow-up study in children with epilepsy.

2.3. Condition: Treatment of epilepsy with partial onset seizures

2.3.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with partial onset seizures.

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

From birth to less than 18 years.

2.3.3. Pharmaceutical form(s)

Film-coated tablet (10 mg, 25 mg and 50 mg), oral solution (1 mg/ml, 10 mg/ml) for oral use, Solution for injection for intravenous use.

2.3.4. Studies

Area	Number of studies	Description
Quality	-	Not applicable.
Non-clinical	3	Same as for condition "Treatment of Paediatric Epilepsy Syndromes"
Clinical	1	**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.

2.4. Condition: Treatment of generalised epilepsy

2.4.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with generalised epilepsy

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

From one month to less than 18 years.

2.4.3. Pharmaceutical form(s)

Film-coated tablet (10 mg, 25 mg and 50 mg), oral solution (1 mg/ml, 10 mg/ml) for oral use, Solution for injection for intravenous use.

2.4.4. Studies

Area	Number of studies	Description
Quality	-	Not applicable.
Non-clinical	3	Same as for condition "Treatment of Paediatric Epilepsy Syndromes".
Clinical	3	**Study 11** Systematic review of the literature of all published trials focusing on the possibility of extrapolating efficacy from adult to paediatric patients with idiopathic generalized epilepsy with primary generalized tonic clonic seizures.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes.
Date of completion of the paediatric investigation plan:	By December 2017.
Deferral for one or more studies contained in the paediatric investigation plan:	Yes.