European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 31 March 2010

on the acceptance of a modification of an agreed Paediatric Investigation Plan for brivaracetam (EMEA-000332-PIP01-08-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.

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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 as amended 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 decision P/126/2009 of the European Medicines Agency issued on 13 July 2009,

Having regard to the application submitted by UCB Pharma S.A. on 7 December 2009 under Article 22 of Regulation (EC) No 1901/2006 as amended proposing changes to the agreed Paediatric Investigation Plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 19 February 2010, in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended,

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

WHEREAS:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to an agreed Paediatric Investigation Plan,

(2) It is therefore appropriate to adopt a Decision on the acceptance of changes to an 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, 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, are hereby accepted.

Article 2

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

Done at London, 31 March 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 February 2010
EMA/171189/2010

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

EMEA-000332-PIP01-08-M01

Scope of the application

Active substance(s):

Brivaracetam

Condition(s):

Paediatric epilepsy syndromes

Neonatal seizures

Epilepsy with partial onset seizures

Idiopathic generalised epilepsy with primary generalised tonic clonic seizures

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.

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 7 December 2009 an application for modification of the agreed

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paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/126/2009 of 13 July 2009. The application for modification proposed changes.

The procedure started on 23 December 2009.

Scope of the modification

Some measures and/or timelines 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 the changes proposed by the applicant regarding the measures and the timelines of the paediatric investigation plan.

   The Icelandic and the Norwegian Paediatric Committee members agree 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, 19 February 2010

On behalf of the Paediatric Committee

Dr Daniel Brasseur, Chairman

(Signature on file)

Annex I

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

A. Condition(s)

Paediatric epilepsy syndromes

Neonatal seizures

Epilepsy with partial onset seizures

Idiopathic generalised epilepsy with primary generalised tonic clonic seizures

B. Waiver

B.1 Condition

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 and 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).

B.2 Condition

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 and 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).

C. Paediatric investigation plan

C.1 Condition to be investigated

Paediatric Epilepsy Syndromes

Proposed PIP indication

Treatment of refractory paediatric epilepsy syndromes with adjunctive administration of brivaracetam.

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

From 1 month to less than 18 years.

Formulation(s)

Film-coated tablet (2.5mg, 10 and 25 mg), oral solution (1 mg/ml, 10 mg/ml) for oral use.

Studies

Area	Number of studies	Description
Quality	**-**	Not applicable.
Non-clinical	**3**	9-week oral toxicity study followed by a 30-day recovery period in juvenile rats. Study to evaluate brain weight in juvenile and adult rats 9-month oral toxicity study in juvenile dogs with a 2-months recovery period.
Clinical	**4**	In silico study for prediction of brivaracetam disposition in children. 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. 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. Open-label, single-arm, long-term follow-up study in children with epilepsy.

C.2 Condition to be investigated

Neonatal Seizures

Proposed PIP indication

Treatment of neonatal seizures with adjunctive administration of brivaracetam.

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

From birth to less than 28 days.

Formulation(s)

Solution for injection, intravenous use.

Studies

Area	Number of studies	Description
Quality		Not applicable.
Non-clinical	**3**	As for Condition 1.
Clinical	**4**	In silico study for prediction of brivaracetam disposition in children. Modelling and simulation of intravenous brivaracetam pharmacokinetic profiles in children to evaluate dose adaptation rules. Open, randomised, parallel group, active controlled study to evaluate efficacy, safety and pharmacokinetics in neonates with repeated seizures Open-label, single-arm, long-term follow-up study in children with epilepsy.

C.3 Condition to be investigated

Epilepsy with partial onset seizures

Proposed PIP indication

Treatment of paediatric patients with partial onset seizures.

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

From birth to less than 18 years.

Formulation(s)

Film-coated tablet (2.5mg, 10 and 25 mg), oral solution (1 mg/ml, 10 mg/ml) for oral use, Solution for injection for intravenous use.

Studies

Area	Number of studies	Description
Quality		Not applicable.
Non-clinical	**3**	As for Condition 1.
Clinical	**1**	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.

C.4 Condition to be investigated

Idiopathic Generalised Epilepsy (IGE) With Primary Generalised Tonic Clonic Seizures (PGTCS)

Proposed PIP indication

Treatment of paediatric patients with IGE with PGTCS.

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

From birth to less than 18 years.

Formulation(s)

Film-coated tablet (2.5mg, 10 and 25 mg), oral solution (1 mg/ml, 10 mg/ml) for oral use, Solution for injection for intravenous use.

Studies

Area	Number of studies	Description
Quality		Not applicable.
Non-clinical	**3**	As for Condition 1.
Clinical	**1**	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.

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	By December 2017
Deferral for some or all studies contained in the paediatric investigation plan:	Yes