European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 12 September 2008

on the application for agreement of a Paediatric Investigation Plan for retigabine (EMEA-000116-PIP01-07) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

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on the application for agreement of a Paediatric Investigation Plan for retigabine (EMEA-000116-PIP01-07) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

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 application submitted by Valeant Pharmaceuticals Ltd. on 13 December 2007 under Article 16(1) also requesting a waiver under Article 13 of said Regulation and a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 31 July 2008, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended, and Article 13 of said Regulation, and Article 21 of said Regulation,

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 a positive opinion,

(2) It is therefore appropriate to adopt a Decision following the Paediatric Committee's opinion on the Paediatric Investigation Plan.

(3) It is therefore appropriate to adopt a Decision granting a waiver.

(4) It is therefore appropriate to adopt a Decision granting a deferral.

HAS ADOPTED THIS DECISION:

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

Article 1

A Paediatric Investigation Plan for retigabine, film-coated tablet, modified-release tablet, age appropriate oral formulation for the age group from 0 to less than 6 years, solution for infusion, oral and 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, is hereby agreed.

Article 2

A waiver for retigabine, film-coated tablet, modified-release tablet, age appropriate oral formulation for the age group from 0 to less than 6 years, solution for infusion, oral and intravenous use, the details of which are set out in the Opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A deferral for retigabine, film-coated tablet, modified-release tablet, age appropriate oral formulation for the age group from 0 to less than 6 years, solution for infusion, oral and intravenous use, the details of which are set out in the Opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Valeant Pharmaceuticals Ltd, Cedarwood, Chineham Business Park, Crockford Lane, Basingstoke, RG24 8WD, United Kingdom.

Done at London, 12 September 2008

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

London, 31 July 2008
Doc. Ref. EMEA/PDCO/386064/2008
EMEA-000116-PIP01-07

POSITIVE OPINION OF THE PAEDIATRIC COMMITTEE ON A REQUEST FOR AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN FOR

Scope of the application

Active substance:
retigabine

Condition(s):
Epilepsy with partial onset seizures
Lennox-Gastaut Syndrome

Pharmaceutical form(s):
film-coated tablet
modified-release tablet
age appropriate oral formulation for the age group from 0 to less than 6 years
solution for infusion

Route(s) of administration:
oral use
intravenous use

Name/corporate name of the PIP applicant:
Valeant Pharmaceuticals Ltd.

Basis for opinion

Pursuant to Article 16.1 of Regulation (EC) No 1901/2006 as amended, Valeant Pharmaceuticals Ltd. submitted for agreement to the EMEA on 13 December 2007 a paediatric investigation plan for the above mentioned medicinal product.

The procedure started on 16 January 2008.

Supplementary information was provided by the applicant on 20 May 2008.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report

- to agree the paediatric investigation plan in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended,
- to grant a deferral in accordance with Article 21 of Regulation (EC) No 1901/2006 as amended,
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of Regulation (EC) No 1901/2006 as amended and concluded in accordance with Article 11(1)(b) of Regulation (EC) No 1901/2006 as amended, on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. 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 are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the Agency, together with its annex(es) and appendix(ces).

London, 31 July 2008

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) / DISEASE(S)

Epilepsy with partial onset seizures
Lennox-Gastaut Syndrome

B. WAIVER

- **Condition**

Lennox-Gastaut syndrome

- **Subset(s) of the paediatric population, pharmaceutical form(s) and route(s) of administration covered**

The waiver applies to:

Newborn infants, Infants & toddlers from the age of 0 to less than 2 years, for film-coated tablet, modified-release tablet, age-appropriate oral formulation for the age group from 0 to less than 6 years, solution for infusion, oral use, intravenous use.

C. PAEDIATRIC INVESTIGATION PLAN

C.1. Condition to be investigated

Epilepsy with partial onset seizures

- **Subset(s) covered**

Newborn infants, infants and toddlers, children and adolescents from 0 to less than 18 years.

- **Formulation(s)**

Film-coated tablet, modified-release tablet, age-appropriate oral formulation for the age group from 0 to less than 6 years, solution for infusion.

- **Studies and measures**

Area	Subarea	Number	Description
Quality	Pharmaceutical Form	1	Development of a film-coated tablet formulation for the paediatric population from 6 years to less than 12 years.
Quality	Pharmaceutical Form	1	Development of an oral age-appropriate formulation for the paediatric population from 0 to less than 6 years.
Quality	Pharmaceutical Form	1	Development of an intravenous formulation for the paediatric population.
Quality	Pharmaceutical Form	1	Development of a modified release tablet formulation for the paediatric population from 6 years to less than 18 years.
Non-clinical	Juvenile animal study	1	12-week oral toxicity study in juvenile rats.
Clinical	pharmacokinetics, safety	1	Open label, single dose PK, safety and tolerability clinical trial in patients aged from 4 years to less than 18 years with partial onset seizures or Lennox-Gastaut Syndrome.

Clinical	pharmacokinetics, safety	1	Open label, multiple dose PK, safety and tolerability clinical trial in patients aged from 4 years to less than 18 years with partial onset seizures or Lennox-Gastaut syndrome.
Clinical	pharmacokinetics, safety	1	Open label, single dose PK, safety and tolerability clinical trial in patients aged from 1 month to less than 4 years with partial onset seizures, Lennox-Gastaut syndrome or infantile spasms.
Clinical	pharmacokinetics, safety	1	Open label, multiple dose PK, safety and tolerability clinical trial in patients aged from 1 month to less than 4 years with partial onset seizures, Lennox-Gastaut syndrome or infantile spasms.
Clinical	pharmacokinetics, safety	1	Open label, PK, safety and tolerability clinical trial in patients aged from 0 to less than 1 month with “multiple seizures”.
Clinical	safety, efficacy	1	Double blind, placebo controlled, multicentre clinical trial for efficacy and safety of retigabine in patients aged from 4 years to less than 18 years for adjunctive therapy of partial onset seizures with open label long-term extension.
Clinical	safety, efficacy	1	Double blind, placebo controlled, multicentre clinical trial for efficacy and safety of retigabine in patients aged from 1 month to less than 4 years for adjunctive therapy of partial onset seizures with open label long-term extension.
Clinical	safety, efficacy	1	Double blind, placebo controlled, multicentre clinical trial for efficacy and safety of retigabine in patients aged from 0 to less than 1 month for adjunctive therapy of “multiple seizures” with open label long-term extension.

C.2. Condition to be investigated

Lennox-Gastaut syndrome

- **Subset(s) covered**

  Children and adolescents from 2 years to less than 18 years.

- **Formulation(s)**

  Film-coated tablet, modified-release tablet, age-appropriate oral formulation for the age group from 0 to less than 6 years, solution for infusion.

- **Studies/measures**

Area	Subarea	Number	Description
Quality	Pharmaceutical Form	4	Measures as described in C.1.
Non-clinical	Juvenile animal study	1	Non-clinical trial as described in C.1.
Clinical	pharmacokinetics, safety	5	Clinical trials as described in C.1.
Clinical	safety, efficacy	1	Double blind, placebo controlled clinical trial of retigabine in patients aged from 4 years to less than 30 years for adjunctive therapy of Lennox-Gastaut syndrome with open label long-term extension.
Clinical	safety, efficacy	1	Double blind, placebo controlled clinical trial of retigabine in patients aged from 2 years to less than 4 years for adjunctive therapy of Lennox-Gastaut syndrome with open label long-term extension.

Need for paediatric measures in an EU Risk Management Plan: **Yes**
Date of completion of Paediatric Investigation Plan: **by September 2015**
A deferral has been granted: **Yes**