EMA/513798/2011

European Medicines Agency decision

P/156/2011

of 4 July 2011

on the acceptance of a modification of an agreed paediatric investigation plan for retigabine (EMEA-000116-PIP01-07-M04) 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 retigabine (EMEA-000116-PIP01-07-M04) 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/77/2008 issued on 12 September 2008, the decision P/153/2009 issued on 9 October 2009, the decision P/35/2010 issued on 31 March 2010, and the decision P/174/2010 issued on 20 September 2010,

Having regard to the application submitted by Glaxo Group Limited on 4 March 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 20 May 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 retigabine, film-coated tablet, modified-release tablet, dispersible/chewable tablet, powder for solution for injection, powder for solution for infusion, 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 Glaxo Group Limited, Glaxo Wellcome House, Berkeley Avenue, UB6 0NN - Greenford, Middlesex, United Kingdom.

Done at London, 4 July 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/PDCO/368422/2011

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

EMEA-000116-PIP01-07-M04

Scope of the application

Active substance(s):

Retigabine

Condition(s):

Epilepsy with partial onset seizures

Lennox-Gastaut Syndrome

Pharmaceutical form(s):

Film-coated tablet

Modified-release tablet

Dispersible/chewable tablet

Powder for solution for injection

Powder for solution for infusion

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

Glaxo Group Limited

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Glaxo Group Limited submitted to the European Medicines Agency on 4 March 2011 an application for modification of the agreed paediatric investigation with a deferral and a waiver as set out in the European Medicines Agency's decision P/77/2008 issued on 12 September 2008, the decision P/153/2009 issued on 9 October 2009, the decision P/35/2010 issued on 31 March 2010 and the decision P/174/2010 issued on 20 September 2010.

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

The procedure started on 23 March 2011.

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 changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

   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, 20 May 2011

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, dispersible/chewable tablet, powder for solution for injection, powder for 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, dispersible/chewable tablet, powder for solution for injection, powder for solution for infusion.

- **Studies and measures**

Area	Subarea	Number	Description
Quality	Pharmaceutical Form	4	Development of a film-coated tablet formulation (12.5 mg, 25 mg) for the paediatric population from 4 years to less than 12 years who can swallow tablets. Development of a dispersible/chewable tablet as the pharmaceutical form for the paediatric population aged from birth to less than 4 years and/or those who are unable to swallow a tablet. Development of an intravenous formulation for the paediatric population from birth to less than 18 years. Development of a pharmaceutical form with modified-release characteristics 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	4	Open-label, multiple dose study to evaluate the pharmacokinetics, safety and tolerability of retigabine as adjunctive treatment in subjects aged from 12 years to less than 18 years with partial onset seizures or Lennox-Gastaut syndrome. Open-label, multiple dose study to evaluate the pharmacokinetics, safety and tolerability of retigabine as adjunctive treatment in subjects aged from 2 years to less than 12 years with partial onset seizures or Lennox-Gastaut syndrome. Open-label, multiple dose study to evaluate the pharmacokinetics, safety and tolerability of retigabine as adjunctive treatment in subjects aged from 1 month to less than 24 months with mixed or partial onset seizures. Open label, single or multiple-dose PK, safety and tolerability study of retigabine as adjunctive treatment in patients aged from birth to less than 1 month of age with multiple seizure types.
Clinical	safety, efficacy	3	Randomised, double-blind, placebo-controlled, multicentre study to evaluate the efficacy and safety of retigabine as adjunctive treatment in patients aged from 2 years to less than 18 years with partial onset seizures. Randomised, double-blind,placebo-controlled multicentre study to evaluate the efficacy and safety of retigabine as adjunctive treatment in patients aged 1

			month to less than 2 years with partial onset seizures. Randomised, double-blind, placebo-controlled, multicentre study to evaluate the efficacy and safety of retigabine as adjunctive treatment in patients from birth to less than 1 month of age with multiple seizure types.
Clinical	long-term safety and efficacy	1	Open-label, uncontrolled extension study to evaluate the long-term safety and efficacy of retigabine in patients who participated in retigabine paediatric studies.

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, dispersible/chewable tablet, powder for solution for injection, powder for 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	4	Clinical trials as described in C.1.
Clinical	safety, efficacy	1	Randomised, double-blind, placebo-controlled, multi-centre, parallel-group clinical trial to evaluate the efficacy and safety of retigabine as adjunctive therapy for Lennox-Gastaut syndrome in patients aged from 2 years to less than 30 years.
Clinical	long-term safety and efficacy	1	Clinical long-term efficacy study as described in C.1.

Measures to address long term follow-up of potential safety issues and efficacy in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2021.
Deferral for some or all studies contained in the paediatric investigation plan:	Yes