EMA/23015/2016

European Medicines Agency decision

P/0009/2016

of 29 January 2016

on the acceptance of a modification of an agreed paediatric investigation plan for retigabine (Trobalt), (EMEA-000116-PIP01-07-M08) 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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An agency of the European Union

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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/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, the decision P/174/2010 issued on 20 September 2010, the decision P/156/2011 issued on 4 July 2011, the decision P/0225/2012 issued on 3 October 2012, the decision issued P/0081/2013 on 27 March 2013, and the decision P/0286/2013 issued on 29 November 2013,

Having regard to the application submitted by Glaxo Group Limited on 18 September 2015 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 11 December 2015, 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 retigabine (Trobalt), film-coated tablet, dispersible/chewable tablet, powder for solution for injection, powder for solution for infusion, 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 Glaxo Group Limited, 980 Great West Road, Middlesex, TW8 9GS - Brentford, United Kingdom.

Done at London, 29 January 2016

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/631862/2015
London, 11 December 2015

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

EMEA-000116-PIP01-07-M08

Scope of the application

Active substance(s):

Retigabine

Invented name:

Trobalt

Condition(s):

Treatment of epilepsy with partial onset seizures

Treatment of Lennox-Gastaut Syndrome

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated 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

Information about the authorised medicinal product:

See Annex II

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 18 September 2015 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/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, the decision P/174/2010 issued on 20 September 2010, the decision P/156/2011 issued on 4 July 2011, the decision P/0225/2012 issued on 3 October 2012, the decision issued P/0081/2013 on 27 March 2013, and the decision P/0286/2013 issued on 29 November 2013.

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

The procedure started on 13 October 2015.

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 Lennox-Gastaut Syndrome

The waiver applies to:

- all subsets of the paediatric population from birth to less than 2 years of age;
- for film-coated tablet, modified-release tablet, dispersible/chewable tablet, powder for solution for injection, powder for solution for infusion, 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 epilepsy with partial onset seizures

2.1.1. Indication(s) targeted by the PIP

Treatment of partial onset seizures with or without secondary generalisation

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Dispersible/chewable tablet

Powder for solution for injection

Powder for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	3	**Study 1** 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. **Study 2** 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.

		Study 3 Development of an intravenous formulation for the paediatric population from birth to less than 18 years. **Study 4** -deleted-
Non-clinical studies	1	**Study 5** 12-week oral toxicity study in juvenile rats.
Clinical studies	11	**Study 6** 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. **Study 7** 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. **Study 8** 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. **Study 9** 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. **Study 10** Open-label, uncontrolled extension study to evaluate the long-term safety and efficacy of retigabine in patients from 12 to less than 18 years who participated in retigabine paediatric studies. **Study 11** Randomised, double-blind, placebo-controlled, multicentre study to evaluate the efficacy and safety of retigabine as adjunctive treatment in patients aged from 12 years to less than 18 years with partial onset seizures. **Study 12** 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.

		Study 13 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. **Study 15** Randomised, double-blind, placebo-controlled, multicentre study to evaluate efficacy and safety of retigabine compared with placebo as adjunctive treatment in patients aged from 2 years to less than 12 years with partial onset seizures. **Study 16** Open-label long-term safety and tolerability study in patients with partial onset seizures (below the age of 12 years) or with Lennox-Gastaut Syndrome (from 2 to less than 30 years of age). **Study 18** Open-label, uncontrolled extension study to evaluate the long-term safety and efficacy of retigabine as adjunctive treatment in POS patients with parital onset seizures (POS) (from 12 to less than 18 years of age) or with Lennox-Gastaut Syndrome (LGS) (12 to less than 30 years of age) who participated in retigabine paediatric studies.

2.2. Condition

Treatment of Lennox-Gastaut Syndrome

2.2.1. Indication(s) targeted by the PIP

Treatment of Lennox-Gastaut Syndrome

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

From 2 to less than 8 years of age

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Dispersible/chewable tablet

Powder for solution for injection

Powder for solution for infusion

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	3	**Studies 1,2,3** as described in condition “Treatment of epilepsy with partial onset seizures”.
Non-clinical studies	1	**Study 5** as described in condition “Treatment of epilepsy with partial onset seizures”.
Clinical studies	9	**Studies 6, 7, 8, 9, 10, 16, 18** as described in condition “Treatment of epilepsy with partial onset seizures”. **Study 14** Randomised, double-blind, placebo-controlled, multi-centre, parallel-group study to evaluate the efficacy and safety of retigabine as adjunctive therapy for Lennox-Gastaut syndrome in patients aged from 12 years to less than 30 years. **Study 17** Randomised, double-blind, placebo-controlled, multi-centre, parallel-group study to evaluate the efficacy and safety of retigabine as adjunctive therapy for Lennox-Gastaut syndrome in patients aged 2 years to less than 12 years.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2035
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 epilepsy with partial-onset seizures

Authorised indications:

- Trobalt is indicated as adjunctive treatment of drug-resistant partial onset seizures with or without secondary generalization in patients aged 18 years or older with epilepsy, where other appropriate drug combinations have proved inadequate or have not been tolerated.

Authorised pharmaceutical formulation(s)

Film-coated tablet

Authorised route(s) of administration

Oral use