EMA/610846/2012

European Medicines Agency decision

P/0225/2012

of 3 October 2012

on the acceptance of a modification of an agreed paediatric investigation plan for retigabine (Trobalt), (EMEA-000116-PIP01-07-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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European Medicines Agency decision

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on the acceptance of a modification of an agreed paediatric investigation plan for retigabine (Trobalt), (EMEA-000116-PIP01-07-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/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 and the decision P/156/2011 issued on 4 July 2011.

Having regard to the application submitted by Glaxo Group Limited on 25 May 2012 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 17 August 2012, 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 (Trobalt), 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, United Kingdom.

Done at London, 3 October 2012

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

EMA/PDCO/362650/2012

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

EMEA-000116-PIP01-07-M05

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

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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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 25 May 2012 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 and the decision P/156/2011 issued on 4 July 2011.

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

The procedure started on 19 June 2012.

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 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, 17 August 2012

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

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 medicinalproduct is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan

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

Modified-release tablet

Dispersible/chewable tablet

Powder for solution for injection

Powder for solution for infusion

2.1.4. Studies

Area	Subarea	Number	Description
Quality	Pharmaceutical Form	4	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 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	Study 5 12-week oral toxicity study in juvenile rats.

Clinical	pharmacokinetics, safety	4	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.
Clinical	safety, efficacy	3	Study 11 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. 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.

Clinical	long-term safety and efficacy	1	Study 10 Open-label, uncontrolled extension study to evaluate the long-term safety and efficacy of retigabine in patients who participated in retigabine paediatric studies.

Condition: Treatment of Lennox-Gastaut Syndrome

2.1.5. Indication(s) targeted by the PIP

Treatment of Lennox-Gastaut Syndrome

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

From 2 to less than 8 years of age.

2.1.7. Pharmaceutical form(s)

Film-coated tablet

Modified-release tablet

Dispersible/chewable tablet

Powder for solution for injection

Powder for solution for infusion

2.1.8. Studies

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	Study 14 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.

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 2021.
Deferral for one or more studies 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 partial onset seizures with or without secondary generalisation in adults aged 18 years and above with epilepsy.

MA (EU) Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Immediate Packaging	Pack size
EU/1/11/681/001	Trobalt	50 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	21 tablets
EU/1/11/681/002	Trobalt	50 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	84 tablets
EU/1/11/681/003	Trobalt	50 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	168 tablets
EU/1/11/681/004	Trobalt	100 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	21 tablets
EU/1/11/681/005	Trobalt	100 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	84 tablets
EU/1/11/681/006	Trobalt	100 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	168 tablets
EU/1/11/681/007	Trobalt	200 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	84 tablets
EU/1/11/681/008	Trobalt	200 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	168 (2 x 84) tablets (multipack)
EU/1/11/681/009	Trobalt	300 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	84 tablets
EU/1/11/681/010	Trobalt	300 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	168 (2 x 84) tablets (multipack)
EU/1/11/681/011	Trobalt	400 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	84 tablets
EU/1/11/681/012	Trobalt	400 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	168 (2 x 84) tablets (multipack)
EU/1/11/681/013	Trobalt	50 mg/100mg	Film-coated tablet	Oral use	blister (PVC/PVDC/Al)	Initiation pack: 21 tablets 50 mg + 42 tablets 100 mg