EMA/519775/2013

European Medicines Agency decision

P/0214/2013

of 3 September 2013

on the agreement of a paediatric investigation plan and on the granting of a deferral for glycerol phenylbutyrate (GPB) (EMEA-000297-PIP02-12) 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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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 application submitted by Hyperion Therapeutics, Ltd. on 21 June 2012 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 19 July 2013, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a 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

A paediatric investigation plan for glycerol phenylbutyrate (GPB), oral liquid, oral use, enteral 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 deferral for glycerol phenylbutyrate (GPB), oral liquid, oral use, enteral 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 granted.

Article 3

This decision is addressed to Hyperion Therapeutics, Ltd., 21 St. Thomas Street, BS1 6JS – Bristol, United Kingdom.

Done at London, 3 September 2013

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

EMA/PDCO/298219/2013

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral

EMEA-000297-PIP02-12

Scope of the application

Active substance(s):

Glycerol phenylbutyrate (GPB)

Condition(s):

Treatment of urea cycle disorders

Pharmaceutical form(s):

Oral liquid

Route(s) of administration:

Oral use

Enteral use

Name/corporate name of the PIP applicant:

Hyperion Therapeutics, Ltd.

Basis for opinion

Pursuant to Article 16(1)of Regulation (EC) No 1901/2006 as amended, Hyperion Therapeutics, Ltd. submitted for agreement to the European Medicines Agency on 21 June 2012 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 9 August 2012.

Supplementary information was provided by the applicant on 22 April 2013. The applicant proposed modifications to the paediatric investigation plan.

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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 said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   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 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 and appendix.

London, 19 July 2013

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

Not applicable.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of urea cycle disorders

2.1.1. Indication(s) targeted by the PIP

Adjunctive therapy for children age with urea cycle disorders involving deficiencies of the following enzymes: carbamyl phosphate synthetase (CPS), ornithine transcarbamylase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL) or arginase (ARG) as well as the mitochondrial transporter ornithine translocase (HHH deficiency).

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)

Oral liquid.

2.1.4. Measures

Area	Number of measures	Description
Quality	1	Measure 1 Development of an age-appropriate liquid form of glycerol phenylbutyrate (GPB).
Non-clinical	0	Not applicable.
Clinical	5	Measure 2 Fixed sequence, open-label, switch-over study of *g*lycerol phenylbutyrate with a long-term safety extension to evaluate the safety, tolerability, PK characteristics, and activity of GPB in children aged from 6 years to less than 18 years for the treatment of urea cycle disorders as compared with sodium phenylbutyrate (NaPBA). Measure 3 Open label safety extension study to evaluate the long-term safety of GPB and its control of blood ammonia in paediatric patients aged from 6 years to less than 18 years with urea cycle disorders. Measure 4 Fixed sequence, open-label, switch-over study of glycerol phenylbutyrate with

Area	Number of measures	Description
		a long-term safety extension to evaluate the safety, tolerability, PK characteristics, and activity of GPB in children aged from 1 month to less than 6 years for the treatment of urea cycle disorders as compared to sodium phenylbutyrate (NaPBA). Measure 5 Open label safety extension study to evaluate the long-term safety of GPB and its control of blood ammonia in paediatric patients aged from 1 month to less than 6 years with urea cycle disorders. Measure 6 Open-label, switch-over, multi-centre, multiple dose, active controlled trial to evaluate pharmacokinetics, safety, efficacy, acceptability/palatability of glycerol phenylbutyrate as add-on to best standard of care compared to sodium phenylbutyrate (NaPBA) in children from birth to less than 2 months of age to age with urea cycle disorders with a 24 months extension phase.

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 December 2016
Deferral for one or more measures contained in the paediatric investigation plan:	Yes