EMA/122586/2014

# European Medicines Agency decision

P/0068/2014

of 14 March 2014

on the acceptance of a modification of an agreed paediatric investigation plan for glycerol phenylbutyrate (EMEA-000297-PIP02-12-M01) 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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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/0214/2013 issued on 4 September 2013,

Having regard to the application submitted by Hyperion Therapeutics, Ltd. on 22 November 2013 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 14 February 2014, 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 glycerol phenylbutyrate, oral liquid, oral use, enteral 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 Hyperion Therapeutics, Ltd., 2000 Sierra Point Parkway, 4th Floor, CA 94005 – Brisbane, United States.

Done at London, 14 March 2014

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

EMA/PDCO/739018/2013

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

EMEA-000297-PIP02-12-M01

## Scope of the application

**Active substance(s):**

Glycerol phenylbutyrate

**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 22 of Regulation (EC) No 1901/2006 as amended, Hyperion Therapeutics, Ltd. submitted to the European Medicines Agency on 22 November 2013 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0214/2013 issued on 4 September 2013.

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

The procedure started on 18 December 2013.

## Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been changed.

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## 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 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, 14 February 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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. Studies

| **Area** | **Number of studies** | **Description** |
|---|---|---|
| Quality | 1 | **Study 1**<br><br>Development of an age-appropriate liquid form of glycerol phenylbutyrate (GPB). |
| Non-clinical | 0 | Not applicable. |
| Clinical | 5 | **Study 2**<br><br>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).<br><br>**Study 3**<br><br>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. |

| Area | Number of studies | Description |
|---|---|---|
| | | **Study 4**<br><br>Fixed sequence, open-label, switch-over study of glycerol phenylbutyrate with 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).<br><br>**Study 5**<br><br>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.<br><br>**Study 6**<br><br>Open-label, multi-centre, multiple dose, non-randomised 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 with urea cycle disorders with an extension phase until the age of 24 months. |

## 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 2018 |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |