EMA/651534/2014

European Medicines Agency decision

P/0314/2014

of 24 November 2014

on the acceptance of a modification of an agreed paediatric investigation plan for heterologous human adult liver-derived progenitor cells (HHALPC) (EMEA-001155-PIP01-11-M02) 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 European Medicines Agency's decision P/0313/2013 issued on 19 December 2013,

Having regard to the application submitted by Promethera Biosciences on 18 July 2014 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 10 October 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 heterologous human adult liver-derived progenitor cells (HHALPC), cell suspension for infusion, 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 Promethera Biosciences, 11, Rue Granbonpré, 1435 - Mont Saint-Guibert, Belgium.

Done at London, 24 November 2014

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

EMA/PDCO/452037/2014

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

EMEA-001155-PIP01-11-M02

Scope of the application

Active substance(s):

Heterologous Human Adult Liver-derived Progenitor Cells (HHALPC)

Condition(s):

Treatment of urea cycle disorders

Treatment of Crigler-Najjar syndrome

Pharmaceutical form(s):

Cell suspension for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Promethera Biosciences

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Promethera Biosciences submitted to the European Medicines Agency on 18 July 2014 an application for modification of the agreed paediatric investigation plan as set out in the European Medicines Agency's decision P/0313/2013 issued on 19 December 2013.

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

The procedure started on 13 August 2014.

Scope of the modification

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

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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 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 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, 10 October 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 (PIP)

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

Treatment of urea cycle disorders

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)

Cell suspension for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality	1	**Study 1** To restrict the concentration of DMSO in the final product for paediatric patients.
Non-clinical	1	**Study 2** Biodistribution, Toxicity and Tumorigenicity study (GLP) in NOD SCID gamma mice / 6 and 8 weeks.
Clinical	4	**Study 3** Prospective multi-centre observational study with a retrospective part in children from birth to less than 18 years of age with urea cycle disorders or Crigler-Najjar syndrome. **Study 4** Dose escalation/safety study in children from birth to less than 18 years of age with urea cycle disorders or Crigler-Najjar syndrome. **Study 7** Safety/efficacy study in children from birth to less than 18 years with urea cycle disorders. **Study 9** Safety/efficacy study of readministration of HHALPC in children from birth to less than 18 years of age with urea cycle disorders and Crigler-Najjar syndrome.

2.2. Condition: treatment of Crigler-Najjar syndrome

2.2.1. Indication(s) targeted by the PIP

Treatment of Crigler-Najjar syndrome

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Cell suspension for infusion

2.2.4. Measures

Area	Number of measures	Description
Quality	1	**Study 1** To restrict the concentration of DMSO in the final product for paediatric patients.
Non-clinical	1	**Study 2** Biodistribution, Toxicity and Tumorigenicity study (GLP) in NOD SCID gamma mice / 6 and 8 weeks.
Clinical	4	**Study 3** Prospective multi-center observational study with a retrospective part in children from birth to less than 18 years of age with urea cycle disorders or Crigler-Najjar syndrome. **Study 4** Dose escalation/safety study in children from birth to less than 18 years of age with urea cycle disorders or Crigler-Najjar syndrome. **Study 8** Safety/efficacy study in children from birth to less than 18 years with Crigler-Najjar syndrome. **Study 9** Safety/efficacy study of readministration of HHALPC in children from birth to less than 18 years of age with urea cycle disorders and Crigler-Najjar syndrome.

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 June 2018
Deferral for one or more measures contained in the paediatric investigation plan:	No