EMA/580078/2016

European Medicines Agency decision

P/0248/2016

of 5 September 2016

on the acceptance of a modification of an agreed paediatric investigation plan for cerliponase alfa (EMEA-001362-PIP01-12-M03) 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/0260/2013 issued on 29 October 2013 and the decision P/0209/2015 issued on 18 September 2015,

Having regard to the application submitted by BioMarin International Limited on 30 May 2016 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 19 August 2016, in accordance with Article 22 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 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 acceptance of changes to the agreed paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision on the granting of a deferral.

(4) It is therefore appropriate to adopt a decision on the refusal of a waiver.

[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 cerliponase alfa, concentrate for solution for infusion, intracerebral 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

A deferral for cerliponase alfa, concentrate for solution for infusion, intracerebral 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

A waiver for cerliponase alfa, concentrate for solution for infusion, intracerebral 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 refused.

Article 4

This decision is addressed to BioMarin International Limited, Shanbally, Ringaskiddy, NA - County Cork, Ireland.

EMA/PDCO/379159/2016
London, 19 August 2016

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

EMEA-001362-PIP01-12-M03

Scope of the application

Active substance(s):

Cerliponase alfa

Condition(s):

Treatment of Neuronal Ceroid Lipofuscinosis type 2

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intracerebral use

Name/corporate name of the PIP applicant:

BioMarin International Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, BioMarin International Limited submitted to the European Medicines Agency on 30 May 2016 an application for modification of the agreed paediatric investigation plan as set out in the European Medicines Agency's decision P/0260/2013 issued on 29 October 2013 and the decision P/0209/2015 issued on 18 September 2015.

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

The procedure started on 21 June 2016.

A meeting with the Paediatric Committee took place on 17 August 2016.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A new study has been added.

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;
   - to grant a deferral, the details of which are set out in the Annex I of this opinion;
   - to refuse the granting of a waiver for some of the subsets of the paediatric population and the above mentioned condition as it does not meet the grounds detailed in Article 11(1) 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 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.

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

For refusing waiver:

The request for the waiver applied to:

- the paediatric population from birth to less than 1 year of age and adolescents from 16 to less than 18 years of age;
- concentrate for solution for infusion, intracerebral use;

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (a) the specific medicinal product is likely to be ineffective or unsafe in the paediatric population.

Because:

- the PDCO disagreed with the applicant's argumentation that the specific medicinal product is likely to be ineffective or unsafe.

The waiver request is therefore refused by the PDCO.

2. Paediatric Investigation Plan

2.1. Condition: treatment of Neuronal Ceroid Lipofuscinosis type 2

2.1.1. Indication(s) targeted by the PIP

Treatment of Late Infantile Neuronal Ceroid Lipofuscinosis type 2 (CLN2) Disease

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)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.

Area	Number of measures	Description
Clinical studies	3	**Study 1** Open-label, dose-escalation trial to evaluate pharmacokinetics, safety, immunogenicity, tolerability and efficacy of multiple doses of cerliponase alfa compared to historical control in children from 3 to less than 16 years of age with Late-Infantile Neuronal Ceroid Lipofuscinosis type 2 (CLN2) Disease. **Study 2** Non interventional natural history study to assess the clinical course of Late Infantile Neuronal Ceroid Lipofuscinosis type 2 (CLN2) Disease. **Study 3** Open-label, multicentre study to evaluate safety, tolerability and efficacy of cerliponase alfa in children from birth to less than 18 years of age with CLN2 Disease.
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

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 July 2020
Deferral for one or more measures contained in the paediatric investigation plan:	Yes