EMA/364928/2015

European Medicines Agency decision

P/0130/2015

of 10 June 2015

on the acceptance of a modification of an agreed paediatric investigation plan for drisapersen (EMEA-000746-PIP01-09-M04) 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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An agency of the European Union

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on the acceptance of a modification of an agreed paediatric investigation plan for drisapersen (EMEA-000746-PIP01-09-M04) 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/54/2011 issued on 4 March 2011, the decision P/255/2011 issued on 26 October 2011, the decision P/0166/2013 issued on 30 July 2013 and the decision P/0342/2014 issued on 12 December 2014,

Having regard to the application submitted by BioMarin International Limited on 2 March 2015 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 22 May 2015, 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 and to the deferral.

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

Changes to the agreed paediatric investigation plan for drisapersen, solution for injection, subcutaneous use, including changes to the deferral, 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 BioMarin International Limited, St. James House, Adelaide Road, 2 Dublin, Ireland.

Done at London, 10 June 2015

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

EMA/PDCO/154768/2015
London, 22 May 2015

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

EMEA-000746-PIP01-09-M04

Scope of the application

Active substance(s):

Drisapersen

Condition(s):

Treatment of Duchenne muscular dystrophy

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous 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 2 March 2015 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/54/2011 issued on 4 March 2011, the decision P/255/2011 issued on 26 October 2011, the decision P/0166/2013 issued on 30 July 2013 and the decision P/0342/2014 issued on 12 December 2014.

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

The procedure started on 24 March 2015.

A meeting with the Paediatric Committee took place on 21 May 2015.

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Scope of the modification

A measure of the Paediatric Investigation Plan has been modified in order to defer the initiation.

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 and to the deferral 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.

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 Duchenne muscular dystrophy

2.1.1. Indication(s) targeted by the PIP

Treatment of patients with Duchenne muscular dystrophy bearing mutations that can be corrected by skipping exon 51

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)

Solution for injection

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	2	**Study 1** Development of the same formulation in a lower strength suitable for the low doses that need to be administered to children below 6 months of age to ensure accuracy of the administered dose. **Study 2** Feasibility of the development of a pre-filled syringe product.
Non-clinical studies	2	**Study 3** 4-week dose ranging and kinetic study by subcutaneous administration in juvenile mice (PND 7) with drisapersen (exon 51 specific phosphorothioate oligonucleotide). Endpoints included clinical observations, body weight (gain), toxicokinetics, and injection site macroscopic pathology. **Study 4** 8-week subcutaneous general juvenile mouse toxicity study including plasma toxicokinetics, developmental immunotoxicity and recovery of any toxicity after 4 weeks off-dose of drisapersen.

Clinical studies	8	**Study 5** Double-blind, escalating dose, randomised, placebo-controlled study to assess the pharmacokinetics, safety and tolerability of drisapersen (exon 51 specific phosphorothioate oligonucleotide) in non-ambulant patients aged 9 years and above with Duchenne muscular dystrophy (DMD114118). **Study 6** Double blind, exploratory, parallel-group, placebo-controlled clinical study to assess two dosing regimens of drisapersen for efficacy, safety, tolerability and pharmacokinetics in ambulant patients 5 years and above with Duchenne muscular dystrophy (DMD114117). **Study 7** Randomised, double blind, placebo-controlled clinical study to assess the efficacy and safety of drisapersen in ambulant patients 5 years and above with Duchenne muscular dystrophy (DMD114044). **Study 8** Double blind, parallel-group, placebo-controlled, exploratory clinical study to assess long-term safety, tolerability, efficacy and pharmacokinetics of drisapersen in non-ambulant patients aged 9 years and above with Duchenne muscular dystrophy (DMD114348). **Study 9** A long-term, open-label safety study of drisapersen in ambulant patients 5 years and above with Duchenne muscular dystrophy for participants in feeder studies e.g. DMD114117 or DMD114044 (DMD114349). **Study 10** Open label, escalating dose ranging study to assess the safety, tolerability, pharmacokinetics and efficacy, of multiple subcutaneous doses of drisapersen in patients with Duchenne muscular dystrophy from birth to below 5 years of age (DMD114402). **Study 11** Randomised, double blind, parallel-group, placebo-controlled confirmatory study to assess the efficacy and safety of drisapersen in non-ambulatory patients with Duchenne muscular dystrophy (identifier not yet assigned). **Study 12** Open-label, natural history-controlled study to assess the efficacy, safety and tolerability of drisapersen in ambulant patients with Duchenne muscular dystrophy (PRO51-CLIN-06).

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 issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2019
Deferral for one or more measures contained in the paediatric investigation plan:	Yes