EMA/275986/2019

European Medicines Agency decision

P/0218/2019

of 17 June 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for adeno-associated viral vector serotype 5 containing a B domain deleted variant of human coagulation factor VIII gene (BMN 270) (EMEA-002427-PIP01-18) 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 BioMarin International Limited on 16 July 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 April 2019, in accordance with Article 17 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 adeno-associated viral vector serotype 5 containing a B domain deleted variant of human coagulation factor VIII gene (BMN 270), solution for infusion, intravenous 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 adeno-associated viral vector serotype 5 containing a B domain deleted variant of human coagulation factor VIII gene (BMN 270), solution for infusion, intravenous 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 BioMarin International Limited, Shanbally, Ringaskiddy , County Cork, P43 R298 – Shanbally, Ireland.

EMA/PDCO/123428/2019
Amsterdam, 26 April 2019

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

EMEA-002427-PIP01-18

Scope of the application

Active substance(s):

Adeno-associated viral vector serotype 5 containing a B domain deleted variant of human coagulation factor VIII gene (BMN 270)

Condition(s):

Treatment of haemophilia A

Pharmaceutical form(s):

Solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

BioMarin International Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, BioMarin International Limited submitted for agreement to the European Medicines Agency on 16 July 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 21 August 2018.

Supplementary information was provided by the applicant on 21 January 2019. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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 17(1) 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.

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 haemophilia A

2.1.1. Indication(s) targeted by the PIP

Treatment of patients with haemophilia A

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 infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	3	**Study 1** Exploratory toxicity and efficacy study comparing FVIII expression levels between neonatal mice and sexually mature mice. **Study 2** Definitive juvenile toxicity study to assess the effect of BMN 270 in mice and to evaluate toxicity during post-natal development at varying ages. **Study 3** Dose range-finding juvenile toxicity study to assess the effects of BMN 270 in mice at the specific ages identified in study 2 and to support dose-selection.
Clinical studies	3	**Study 4** Open-label, single-arm, single dose trial to evaluate safety and efficacy of BMN 270 in children from 12 years to less than 18 years of age with haemophilia A.

		Study 5 Open-label, single-arm, single dose trial to evaluate safety and efficacy of BMN 270 in children from 6 years to less than 12 years of age with haemophilia A. **Study 6** Open-label, single-arm, single dose trial to evaluate safety and efficacy of BMN 270 in children from birth to less than 6 years of age with haemophilia A.
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/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2035
Deferral for one or more measures contained in the paediatric investigation plan:	Yes