EMA/429873/2023

European Medicines Agency decision

P/0410/2023

of 27 October 2023

on the acceptance of a modification of an agreed paediatric investigation plan for fitusiran (EMEA-001855-PIP01-15-M05) 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.

European Medicines Agency decision

P/0410/2023

of 27 October 2023

on the acceptance of a modification of an agreed paediatric investigation plan for fitusiran (EMEA-001855-PIP01-15-M05) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0186/2019 issued on 15 May 2019, the decision P/0424/2019 issued on 4 December 2019, the decision P/0302/2020 issued on 12 August 2020 and the decision P/0109/2023 issued on 14 April 2023,

Having regard to the application submitted by Genzyme Europe B.V. on 26 May 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 8 September 2023, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for fitusiran, 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 Sanofi B.V., 25 Paasheuvelweg, 1105 BP - Amsterdam The Netherlands.

EMA/PDCO/261392/2023
Amsterdam, 8 September 2023

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

EMEA-001855-PIP01-15-M05

Scope of the application

Active substance(s):

Fitusiran

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of congenital haemophilia A

Treatment of congenital haemophilia B

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Sanofi B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Genzyme Europe B.V. submitted to the European Medicines Agency on 26 May 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0186/2019 issued on 15 May 2019, the decision P/0424/2019 issued on 4 December 2019, the decision P/0302/2020 issued on 12 August 2020 and the decision P/0109/2023 issued on 14 April 2023.

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

The procedure started on 10 July 2023.

On 31 August 2023 Genzyme Europe B.V. requested to transfer the paediatric investigation plan to Sanofi B.V.

Scope of the modification

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

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 Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver 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 annexes 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

1.1. Condition

Treatment of congenital haemophilia A

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- solution for injection, subcutaneous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1.2. Condition

Treatment of congenital haemophilia B

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- solution for injection, subcutaneous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of congenital haemophilia A

2.1.1. Indication(s) targeted by the PIP

Routine prophylaxis to prevent or reduce the frequency of bleeding episodes in children aged $\geqslant$ 1 year with severe congenital haemophilia A, including patients who express neutralizing antibodies to exogenous factor VIII substitution

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

From 1 year to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** Dose range-finding juvenile toxicity study to evaluate the potential toxicity of fitusiran in neonate Sprague-Dawley rats (9000727)
Clinical studies	**Study 2** Randomized, open-label, parallel group study comparing fitusiran to on-demand bypassing agents (BPA) in patients from 12 years to less than 18 years of age (and adults) with haemophilia A or B who express inhibitors to replacement factor therapy and who receive on demand treatment for bleeding episodes. The objectives are to evaluate efficacy, safety, PK, PD and HRQoL (ALN-AT3SC-003; Sanofi Genzyme EFC14768) **Study 3** Randomized, open-label, parallel group study comparing fitusiran to on-demand factor VIII or IX only in patients from 12 years to less than 18 years of age (and adults) with haemophilia A or B without inhibitors to replacement factor therapy and who receive on demand treatment for bleeding episodes. The objectives are to evaluate efficacy, safety, PK, PD and HRQoL (ALN-AT3SC-004; Sanofi Genzyme EFC14769). **Study 4** Open-label, single-arm, one-way crossover study initiated for haemophilia A and B patients from 12 years to less than 18 years of age (and adults) with and without inhibitors, previously treated with prophylactic Factor VIII or Factor IX or bypassing agents (BPAs). Intra patient comparison of patients treated with fitusiran to previous standard of care prophylaxis treatment (run-in period). The objective of the study is to assess the efficacy and safety of fitusiran administration as prophylaxis (ALN-AT3SC-009; Sanofi Genzyme EFC15110) **Study 5** Open-label extension study with patients from studies ALN-AT3SC-003, ALN-AT3SC-004 and ALN-AT3SC-009. The main objective of the study is to assess the efficacy and safety of long-term administration of fitusiran (LTE15174)

	Study 6 Open-label, non-comparative study in patients from 1 year to less than 12 years of age with severe haemophilia A or B who express inhibitors to replacement factor therapy and who receive on demand treatment for bleeding episodes. The objectives are to evaluate safety, PK and PD (ATLAS Paediatrics Study Part A, EFC15467). **Study 7** *Deleted in EMEA-001855-PIP01-15-M05.* **Study 8** Open label, single arm study in patients from 1 year to less than 12 years of age with severe haemophilia A or B, with and without inhibitors, previously receiving prophylactic factor VIII/IX or bypassing agent treatment. Intra patient comparison of fitusiran treatment period versus standard of care period prior to enrollment, based on pre- study bleed data. The objectives are to evaluate efficacy and safety of fitusiran administration as prophylaxis (ATLAS Paediatrics Study Part B, EFC15467) **Study 9** *Added in EMEA-001855-PIP01-15-M05.* Open-label, single-arm, one-way crossover study to evaluate the efficacy and safety of fitusiran prophylaxis in male participants aged from12 years to less than 18 years of age (and adults) with severe haemophilia A or B, with or without inhibitory antibodies to factor VIII or IX, who have switched from their prior Clotting Factor Concentrate (CFC) or Bypassing Agents (BPA) standard of care treatment (ATLAS NEO, EFC17574)
Extrapolation, modelling and simulation studies	Not applicable
Other studies	Not applicable
Other measures	Not applicable

2.2. Condition

Treatment of congenital haemophilia B

2.2.1. Indication(s) targeted by the PIP

Routine prophylaxis to prevent or reduce the frequency of bleeding episodes in children aged ⩾ 1 year with severe congenital haemophilia B, including patients who express neutralizing antibodies to exogenous factor IX substitution

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

From 1 year to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Solution for injection

2.2.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** Same as Study 1 for *Treatment of congenital Haemophilia A*
Clinical studies	**Study 2** Same as Study 2 for *Treatment of congenital Haemophilia A* **Study 3** Same as Study 3 for *Treatment of congenital Haemophilia A* **Study 4** Same as Study 4 for *Treatment of congenital Haemophilia A* **Study 5** Same as Study 5 for *Treatment of congenital Haemophilia A* **Study 6** Same as Study 6 for *Treatment of congenital Haemophilia A* **Study 7** *Deleted in EMEA-001855-PIP01-15-M05.* **Study 8** Same as Study 8 for *Treatment of congenital Haemophilia A* **Study 9** *Added in EMEA-001855-PIP01-15-M05.*

	Same as Study 9 for Treatment of congenital Haemophilia A
Extrapolation, modelling and simulation studies	Not applicable
Other studies	Not applicable
Other measures	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 June 2030
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.