EMA/347165/2023

European Medicines Agency decision

P/0358/2023

of 8 September 2023

on the acceptance of a modification of an agreed paediatric investigation plan for concizumab (EMEA-002326-PIP04-20-M01) 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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on the acceptance of a modification of an agreed paediatric investigation plan for concizumab (EMEA-002326-PIP04-20-M01) 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/0371/2021 issued on 8 September 2021,

Having regard to the application submitted by Novo Nordisk A/S on 24 April 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 21 July 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.

(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, 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 concizumab, solution for injection in pre-filled pen, subcutaneous 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 Novo Nordisk A/S, Novo Allé 1, 2880 – Bagsværd, Denmark.

EMA/PDCO/214906/2023
Amsterdam, 21 July 2023

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

EMEA-002326-PIP04-20-M01

Scope of the application

Active substance(s):

Concizumab

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 in pre-filled pen

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Novo Nordisk A/S

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novo Nordisk A/S submitted to the European Medicines Agency on 24 April 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/0371/2021 issued on 8 September 2021.

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

The procedure started on 22 May 2023.

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 in the scope set out in the Annex I of this opinion.
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 does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

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 does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of congenital haemophilia A

2.1.1. Indication(s) targeted by the PIP

Prophylaxis of bleeding episodes in patients with congenital haemophilia A (factor VIII deficiency), with and without inhibitors

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	Not applicable.
Clinical studies	**Study 1 (NN7415-4311)** Randomised, open label, active-control study to assess efficacy, safety and pharmacokinetics of concizumab prophylaxis as compared to no prophylaxis (bypassing agent on-demand) in congenital haemophilia A and B patients with inhibitors from 12 years to less than 18 years of age (and adults). **Study 2 (NN7415-4307)** Randomised, open label, active-control study to assess efficacy, safety and pharmacokinetics of concizumab prophylaxis as compared to no prophylaxis (factor products on-demand) and to prophylaxis with factor VIII or factor IX in patients with congenital severe haemophilia A or moderate/severe haemophilia B without inhibitors from 12 years to less than 18 years of age (and adults). **Study 3 (NN7415-4616)** Non-randomised, open-label intra-patient controlled, single-arm study with age staggered enrolment, to evaluate efficacy, safety and pharmacokinetics of concizumab prophylaxis versus previous standard of care on-demand and prophylaxis treatment in congenital haemophilia A and B patients with and without inhibitors from 1 year to less than 12 years of age.
Extrapolation, modelling and simulation studies	**Study 4** Population PK Modelling and Simulation study to evaluate a suitable dose of concizumab for children from 1 year to less than 18 years of age. **Study 5** Exploratory analysis investigating the relationship between predicted concizumab exposure and treated bleeds.
Other studies	**Study 6** *Study added during procedure EMEA-002326-PIP04-20-M01* Non-comparative, open label compassionate use programme for patients with congenital haemophilia who cannot be treated satisfactorily with authorised and marketed medicines, and who are not able to enrol in clinical trials designed to support the development and registration of concizumab.
Other measures	Not applicable.

2.2. Condition:

Treatment of congenital haemophilia B

2.2.1. Indication(s) targeted by the PIP

Prophylaxis of bleeding episodes in patients with congenital haemophilia B (factor IX deficiency), with and without inhibitors

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	Not applicable.
Clinical studies	**Study 1** *Same as for condition Treatment of congenital haemophilia A, see above* **Study 2** *Same as for condition Treatment of congenital haemophilia A, see above* **Study 3** *Same as for condition Treatment of congenital haemophilia A, see above*
Extrapolation, modelling and simulation studies	**Study 4** *Same as for condition Treatment of congenital haemophilia A, see above* **Study 5** *Same as for condition Treatment of congenital haemophilia A, see above*
Other studies	**Study 6** *Study added during procedure EMEA-002326-PIP04-20-M01* *Same as for condition Treatment of congenital haemophilia A, see above*
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 January 2027
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.