MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-100372-PIP01-21) and to the deferral

MHRA-100372-PIP01-21-M01

Scope of the Application

Active Substance(s)

concizumab

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 Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Novo Nordisk Limited submitted to the licensing authority on 09/08/2023 12:58 BST an application for a

The procedure started on 01/12/2023 10:02 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100372-PIP01-21-M01

Of 13/02/2024 09:17 GMT

On the adopted decision for concizumab (MHRA-100372-PIP01-21-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a for concizumab , Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Novo Nordisk Limited, CMR, 3 City Place, Beehive Ring Road, Gatwick, UNITED KINGDOM, RH6 0PA

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of congenital haemophilia A The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Solution for injection Route(s) of administration: Subcutaneous use Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible. Condition 2: Treatment of congenital haemophilia B The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Solution for injection Route(s) of administration: Subcutaneous use Reason for granting waiver: 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(s):

Condition 1: Treatment of congenital haemophilia A Condition 2: Treatment of congenital haemophilia B

2.2 Indication(s) targeted by the PIP:

Condition 1: Prophylaxis of bleeding episodes in patients with congenital haemophilia A (factor VIII deficiency), with and without inhibitors Condition 2: Prophylaxis of bleeding episodes in patients with congenital haemophilia B (factor IX deficiency), with and without inhibitors

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

For both Conditions: The paediatric population from 1 year to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both Conditions: Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	4	(Same studies for both Conditions) Study 1 (NN7415-4311) Randomised, open label, active-control study to assess efficacy, safety and PK of concizumab prophylaxis as compared to no prophylaxis (bypassing agent on-demand) in patients with haemophilia A or B 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 PK 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 safety, efficacy and pharmacokinetics of concizumab prophylaxis versus previous standard of care on-demand and prophylaxis treatment in congenital haemophilia A and B with and without inhibitors, from 1 year to less than 12 years of age. Study 6 (NN7415-4807) (Added during procedure MHRA-00372-PIP01-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.
Extrapolation, Modeling & Simulation Studies	2	(Same studies for both Conditions) 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	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	31/01/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes