



## Clinical trial results:

### Safety of turoctocog alfa for prophylaxis and treatment of bleeding episodes in previously treated patients with moderate or severe haemophilia A in India

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-002281-46 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 22 April 2019  |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 25 October 2019 |
| First version publication date | 25 October 2019 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | NN7008-4304 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT03449342     |
| WHO universal trial number (UTN)   | U1111-1179-5950 |

Notes:

##### Sponsors

|                              |                                                                                                   |
|------------------------------|---------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Novo Nordisk A/S                                                                                  |
| Sponsor organisation address | Novo Allé, Bagsvaerd, Denmark, 2880                                                               |
| Public contact               | Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |
| Scientific contact           | Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |

Notes:

##### Paediatric regulatory details

|                                                                      |     |
|----------------------------------------------------------------------|-----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No  |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

|                                                      |                |
|------------------------------------------------------|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 26 August 2019 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 25 March 2019  |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 22 April 2019  |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To assess safety of turoctocog alfa during treatment and prophylaxis of bleeding episodes in previously treated patients with moderate or severe haemophilia A in India

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki and ICH Good Clinical Practice, including archiving of essential documents.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 23 February 2018 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | India: 60 |
| Worldwide total number of subjects   | 60        |
| EEA total number of subjects         | 0         |

Notes:

### Subjects enrolled per age group

|                                           |    |
|-------------------------------------------|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 10 |
| Adults (18-64 years)                      | 50 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at 10 sites in India.

### Pre-assignment

Screening details:

A washout period for a minimum of 72 hours for factor 8 (FVIII) containing products prior to collection of FVIII activity and FVIII inhibitor laboratory samples at visit 1 (screening) was done to ensure subject eligibility. Prior to visit 4 (end of trial), a washout of minimum 48 hours was done to avoid interference with the FVIII inhibitor assay

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

Blinding implementation details:

Not applicable

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Adolescents (12 - <18 years) |
|------------------|------------------------------|

Arm description:

Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks.

|                                        |                                               |
|----------------------------------------|-----------------------------------------------|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | TUROCTOCOG ALFA                               |
| Investigational medicinal product code |                                               |
| Other name                             | NovoEight®                                    |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intravenous use                               |

Dosage and administration details:

Dosing for prophylaxis was according to the approved prescribing information. The recommended frequency of dosing could be either every second day or 3 times weekly, at a dose in the range of 20-50 IU/kg. Bleeds were treated with one or more turoctocog alfa intravenous (i.v.) bolus injections. The individual dose levels were decided by the investigator based on recommendations from the World Federation of Hemophilia (WFH). Participants who underwent surgery were treated with turoctocog alfa according to WFH recommendations and the following guidance: Minor surgery; to maintain FVIII activity levels at 30–60 IU/dL.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Adults (≥18 years) |
|------------------|--------------------|

Arm description:

Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks.

|                                        |                                               |
|----------------------------------------|-----------------------------------------------|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | TUROCTOCOG ALFA                               |
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Dosing for prophylaxis was according to the approved prescribing information. The recommended

frequency of dosing could be either every second day or 3 times weekly, at a dose in the range of 20-50 IU/kg. Bleeds were treated with one or more turoctocog alfa i.v. bolus injections. The individual dose levels were decided by the investigator based on recommendations from the WFH. Participants who underwent surgery were treated with turoctocog alfa according to WFH recommendations and the following guidance: Minor surgery; to maintain FVIII activity levels at 30–60 IU/dL.

| <b>Number of subjects in period 1</b> | Adolescents (12 - <18 years) | Adults (≥18 years) |
|---------------------------------------|------------------------------|--------------------|
| Started                               | 10                           | 50                 |
| Completed                             | 10                           | 50                 |

## Baseline characteristics

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Adolescents (12 - <18 years) |
|-----------------------|------------------------------|

Reporting group description:

Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Adults (≥18 years) |
|-----------------------|--------------------|

Reporting group description:

Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks.

| Reporting group values                | Adolescents (12 - <18 years) | Adults (≥18 years) | Total |
|---------------------------------------|------------------------------|--------------------|-------|
| Number of subjects                    | 10                           | 50                 | 60    |
| Age Categorical<br>Units: Subjects    |                              |                    |       |
| Adolescents (12-17 years)             | 10                           | 0                  | 10    |
| Adults (18-64 years)                  | 0                            | 50                 | 50    |
| Age Continuous<br>Units: years        |                              |                    |       |
| arithmetic mean                       | 13.90                        | 27.10              |       |
| standard deviation                    | ± 1.91                       | ± 7.28             | -     |
| Gender Categorical<br>Units: Subjects |                              |                    |       |
| Male                                  | 10                           | 50                 | 60    |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                         |                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                   | Adolescents (12 - <18 years) |
| Reporting group description:<br>Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks. |                              |
| Reporting group title                                                                                                                                                                                                                                                                   | Adults (≥18 years)           |
| Reporting group description:<br>Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks. |                              |

### Primary: Occurrence of confirmed FVIII inhibitor development (≥ 0.6 BU)

|                                                                                                                                                                                                                                                                                        |                                                                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                        | Occurrence of confirmed FVIII inhibitor development (≥ 0.6 BU) <sup>[1]</sup> |
| End point description:<br>The number of participants who confirmed the presence of FVIII inhibitor development (≥ 0.6 BU) during the trial. Results are based on the full analysis set (FAS), that included all dosed participants with data after dosing during 8 weeks of treatment. |                                                                               |
| End point type                                                                                                                                                                                                                                                                         | Primary                                                                       |
| End point timeframe:<br>During 8 weeks of treatment                                                                                                                                                                                                                                    |                                                                               |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The primary endpoint investigated safety and was analysed using descriptive statistics, and thus no statistical analysis was performed.

| End point values                             | Adolescents<br>(12 - <18<br>years) | Adults (≥18<br>years) |  |  |
|----------------------------------------------|------------------------------------|-----------------------|--|--|
| Subject group type                           | Reporting group                    | Reporting group       |  |  |
| Number of subjects analysed                  | 10                                 | 50                    |  |  |
| Units: Participants                          |                                    |                       |  |  |
| Number of subjects with inhibitor antibodies | 0                                  | 0                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Frequency of adverse drug reactions (AR) and serious adverse reactions (SAR)

|                                                                                                                                                                                                                                                                                                                                              |                                                                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                              | Frequency of adverse drug reactions (AR) and serious adverse reactions (SAR) |
| End point description:<br>Frequency of adverse drug reactions (ARs) and serious adverse reactions (SARs) are presented as rate of events, which was calculated as the number of ARs per patient years. All presented ARs and SARs are treatment emergent and related to trial product, which were defined as the events reported after trial |                                                                              |

product administration until the follow-up, 12 weeks after first treatment. Results are based on the safety analysis set, that included all dosed participants with data after dosing during 8 weeks of treatment.

|                                                          |           |
|----------------------------------------------------------|-----------|
| End point type                                           | Secondary |
| End point timeframe:                                     |           |
| Reported until follow-up, 12 weeks after first treatment |           |

| End point values            | Adolescents<br>(12 - <18<br>years) | Adults (≥18<br>years) |  |  |
|-----------------------------|------------------------------------|-----------------------|--|--|
| Subject group type          | Reporting group                    | Reporting group       |  |  |
| Number of subjects analysed | 10                                 | 50                    |  |  |
| Units: Rate of reactions    |                                    |                       |  |  |
| number (not applicable)     |                                    |                       |  |  |
| Adverse drug reactions      | 0                                  | 0                     |  |  |
| Serious adverse reactions   | 0                                  | 0                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Successful haemostatic effect of turoctocog alfa in the treatment of bleeding episodes

|                 |                                                                                        |
|-----------------|----------------------------------------------------------------------------------------|
| End point title | Successful haemostatic effect of turoctocog alfa in the treatment of bleeding episodes |
|-----------------|----------------------------------------------------------------------------------------|

End point description:

The haemostatic effect of turoctocog alfa when used for treatment of bleeding episodes was evaluated during 8 weeks of treatment. Results are based on the FAS that included all dosed participants with data after dosing during 8 weeks of treatment.

|                             |           |
|-----------------------------|-----------|
| End point type              | Secondary |
| End point timeframe:        |           |
| During 8 weeks of treatment |           |

| End point values              | Adolescents<br>(12 - <18<br>years) | Adults (≥18<br>years) |  |  |
|-------------------------------|------------------------------------|-----------------------|--|--|
| Subject group type            | Reporting group                    | Reporting group       |  |  |
| Number of subjects analysed   | 3 <sup>[2]</sup>                   | 46 <sup>[3]</sup>     |  |  |
| Units: % of bleeding episodes |                                    |                       |  |  |
| number (not applicable)       | 66.7                               | 82.6                  |  |  |

Notes:

[2] - Number of subjects analysed = number of bleeding episodes treated with turoctocog alfa

[3] - Number of subjects analysed = number of bleeding episodes treated with turoctocog alfa

### Statistical analyses

No statistical analyses for this end point

### Secondary: Total annualised consumption of turoctocog alfa

|                 |                                                 |
|-----------------|-------------------------------------------------|
| End point title | Total annualised consumption of turoctocog alfa |
|-----------------|-------------------------------------------------|

End point description:

Total consumption of turoctocog alfa (IU/kg body weight (BW) per year) per participant was evaluated during 8 weeks of treatment. Results are based on the FAS that included all dosed participants with data after dosing during 8 weeks of treatment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Measured during the 8 weeks of treatment

| End point values                     | Adolescents<br>(12 - <18<br>years) | Adults (≥18<br>years) |  |  |
|--------------------------------------|------------------------------------|-----------------------|--|--|
| Subject group type                   | Reporting group                    | Reporting group       |  |  |
| Number of subjects analysed          | 10                                 | 50                    |  |  |
| Units: IU/kg BW/year/participant     |                                    |                       |  |  |
| arithmetic mean (standard deviation) | 7030 (± 1053)                      | 6086 (± 1735)         |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Frequency of allergic or infusion reactions related to the trial product

|                 |                                                                          |
|-----------------|--------------------------------------------------------------------------|
| End point title | Frequency of allergic or infusion reactions related to the trial product |
|-----------------|--------------------------------------------------------------------------|

End point description:

Frequency of allergic or infusion reactions related to trial products are presented as rate of adverse reactions, which was calculated as the number of reactions per patient years. Allergic reactions are a class of adverse events related to allergy. Results are based on the safety analysis set, that included all dosed participants with data after dosing during 8 weeks of treatment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Reported until follow-up, 12 weeks after first treatment

| End point values                 | Adolescents<br>(12 - <18<br>years) | Adults (≥18<br>years) |  |  |
|----------------------------------|------------------------------------|-----------------------|--|--|
| Subject group type               | Reporting group                    | Reporting group       |  |  |
| Number of subjects analysed      | 10                                 | 50                    |  |  |
| Units: Rate of adverse reactions |                                    |                       |  |  |
| number (not applicable)          | 0                                  | 0                     |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Week 0 - 12 (8 weeks of treatment period + 4 weeks of follow-up period).

Adverse event reporting additional description:

All the adverse events are based on the SAS which included all dosed participants with data after dosing. 'Number of deaths causally related to treatment' is the data considered to present under 'total number of deaths resulting from adverse events'.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |    |
|--------------------|----|
| Dictionary version | 21 |
|--------------------|----|

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Adolescents (12 - <18 years) |
|-----------------------|------------------------------|

Reporting group description:

Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Adults (≥18 years) |
|-----------------------|--------------------|

Reporting group description:

Participants were to receive preventive turoctocog alfa at a frequency of 'every second day' or '3 times a week' at a dose in the range of 20-50 IU/kg at the investigator's discretion. The total treatment duration for each participant was 8 weeks.

| Serious adverse events                            | Adolescents (12 - <18 years) | Adults (≥18 years) |  |
|---------------------------------------------------|------------------------------|--------------------|--|
| Total subjects affected by serious adverse events |                              |                    |  |
| subjects affected / exposed                       | 0 / 10 (0.00%)               | 0 / 50 (0.00%)     |  |
| number of deaths (all causes)                     | 0                            | 0                  |  |
| number of deaths resulting from adverse events    | 0                            | 0                  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | Adolescents (12 - <18 years) | Adults (≥18 years) |  |
|-------------------------------------------------------|------------------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                              |                    |  |
| subjects affected / exposed                           | 2 / 10 (20.00%)              | 2 / 50 (4.00%)     |  |
| Nervous system disorders                              |                              |                    |  |
| Headache                                              |                              |                    |  |
| subjects affected / exposed                           | 1 / 10 (10.00%)              | 0 / 50 (0.00%)     |  |
| occurrences (all)                                     | 1                            | 0                  |  |
| Infections and infestations                           |                              |                    |  |

|                                                                                       |                      |                     |  |
|---------------------------------------------------------------------------------------|----------------------|---------------------|--|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>2 | 2 / 50 (4.00%)<br>2 |  |
|---------------------------------------------------------------------------------------|----------------------|---------------------|--|

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported