



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/646736/2013

European Medicines Agency decision

P/0277/2013

of 24 October 2013

on the acceptance of a modification of an agreed paediatric investigation plan for insulin degludec (Tresiba) (EMA-000456-PIP01-08-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.



European Medicines Agency decision

P/0277/2013

of 24 October 2013

on the acceptance of a modification of an agreed paediatric investigation plan for insulin degludec (Tresiba) (EMA-000456-PIP01-08-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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/44/2010 issued on 31 March 2010,

Having regard to the application submitted by Novo Nordisk A/S on 13 September 2013 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 11 October 2013, 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.

² OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for insulin degludec (Tresiba), 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 Novo Nordisk A/S, Novo Allé, DK-2880 – Bagsværd, Denmark.

Done at London, 24 October 2013

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/601363/2013

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-000456-PIP01-08-M01

Scope of the application

Active substance(s):

Insulin degludec

Invented name:

Tresiba

Condition(s):

Treatment of type I diabetes mellitus

Treatment of type II diabetes mellitus

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name / corporate name of the PIP applicant:

Novo Nordisk A/S

Information about the authorised medicinal product:

See Annex II

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 13 September 2013 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/44/2010 issued on 31 March 2010.

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

The procedure started on 10 October 2013.

Scope of the modification

Some 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 Norwegian Paediatric Committee member 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.

London, 11 October 2013

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

1. Waiver

1.1. Condition: treatment of type I diabetes mellitus

The waiver applies to:

- Neonates and infants from birth to less than 12 months of age;
- for LysB29(Nε-hexadecandioyl-γ-Glu) des(B30) human insulin, solution for injection, subcutaneous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset.

1.2. Condition: treatment of type II diabetes mellitus

The waiver applies to:

- Children from birth to less than 10 years of age;
- for LysB29(Nε-hexadecandioyl-γ-Glu) des(B30) human insulin, solution for injection, subcutaneous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset.

2. Paediatric Investigation Plan

2.1. Condition: treatment of type I diabetes mellitus

2.1.1. Indication(s) targeted by the PIP

Treatment of type I diabetes mellitus

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

From 1 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Solution for injection, subcutaneous use, in pre-filled disposable injector

2.1.4. Measures

Area	Number of measures	Description
Quality	1	Measure 1: Availability of a dispensing system capable of delivering insulin doses in 0.5 U steps.
Non-clinical		Not applicable.

Clinical	4	Measure 2: Randomised, single-centre, double-blind, two-period cross-over, single-dose trial investigating the pharmacokinetic properties of LysB29(Nε-hexadecandioyl-γ-Glu) des(B30) human insulin and insulin glargine in children from 6 to less than 18 years of age (and in adults) with type I diabetes mellitus. Measure 3: Randomised, open-label, parallel-group, 6-month efficacy and safety non-inferiority study of LysB29(Nε-hexadecandioyl-γ-Glu) des(B30) human insulin and insulin detemir, both in combination with mealtime insulin aspart, in children and adolescents with type I diabetes mellitus, from 1 to less than 18 years of age, followed by a 6-month extension for further evaluation of safety and immunogenicity. Measure 4: PK/PD modelling study in children from 1 to less than 18 years of age, with type I diabetes mellitus. Measure 5: Bioequivalence study in adults of insulin 454 drug substance manufactured for phase 2 with <i>S. cerevisiae</i> strain MT748 and insulin 454 drug substance manufactured for phase 3 with <i>S. cerevisiae</i> strain NN729.
----------	---	---

2.2. Condition: treatment of type II diabetes mellitus

2.2.1. Indication(s) targeted by the PIP

Treatment of type II diabetes mellitus

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

From 10 to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Solution for injection, subcutaneous use, in pre-filled disposable injector

2.2.4. Measures

Area	Number of measures	Description
Quality	1	Measure 1: Availability of a dispensing system capable of delivering insulin doses in 0.5 U steps.
Non-clinical		Not applicable.

Clinical	5	Measure 2: Randomised, single-centre, double-blind, two-period cross-over, single-dose trial investigating the pharmacokinetic properties of LysB29(Nε-hexadecandioyl-γ-Glu) des(B30) human insulin and insulin glargine in children from 6 to less than 18 years of age (and in adults) with type I diabetes mellitus. (same as for condition 1). Measure 3: Randomised, open-label, parallel-group, 6-month efficacy and safety non-inferiority study of LysB29(Nε-hexadecandioyl-γ-Glu) des(B30) human insulin and insulin detemir, both in combination with mealtime insulin aspart, in children and adolescents with type I diabetes mellitus, from 1 to less than 18 years of age, followed by a 6-month extension for further evaluation of safety and immunogenicity. (same as for condition 1) Measure 4: PK/PD modelling study in children from 1 to less than 18 years of age, with type I diabetes mellitus. (same as for condition 1) Measure 5: Bioequivalence study in adults of insulin 454 drug substance manufactured for phase 2 with <i>S. cerevisiae</i> strain MT748 and insulin 454 drug substance manufactured for phase 3 with <i>S. cerevisiae</i> strain NN729. (same as for condition 1) Measure 6: Extrapolation and modelling study, to extend efficacy results in adults with type 2 diabetes mellitus and in adolescents with type 1 diabetes mellitus, to adolescents with type 2 diabetes mellitus.
----------	---	---

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By August 2013
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of diabetes mellitus.

Authorised indication(s):

- Treatment of diabetes mellitus in adults.

Authorised pharmaceutical form(s):

Solution for injection.

Authorised route(s) of administration:

Subcutaneous administration.