EMA/190278/2010

European Medicines Agency decision

P/44/2010

of 31 March 2010

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for Insulin degludec (EMEA-000456-PIP01-08) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8670
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

European Medicines Agency decision

P/44/2010

of 31 March 2010

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for Insulin degludec(EMEA-000456-PIP01-08) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Novo Nordisk A/S on 4 December 2008 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 19 February 2010, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for Insulin degludec, solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for Insulin degludec, solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for Insulin degludec, solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.

Done at London, 31 March 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMA/PDCO/845526/2009
EMEA-000456-PIP01-08

OPINION OF THE PAEDIATRIC COMMITTEE ON THE AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN AND A DEFERRAL AND A WAIVER

Scope of the application

Active substance(s):
Insulin degludec

Condition(s):
Type I diabetes mellitus
Type II diabetes mellitus

Pharmaceutical form(s):
Solution for injection

Route(s) of administration:
Subcutaneous use

Name/corporate name of the PIP applicant:
Novo Nordisk A/S

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novo Nordisk A/S submitted for agreement to the EMEA on 4 December 2008 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 8 January 2009.

Supplementary information was provided by the applicant on 7 December 2009

A meeting with the Paediatric Committee took place on 17 February 2010.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
- to grant a deferral in accordance with Article 21 of said Regulation;
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients, and in accordance with Articles 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

The Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 Agency, together with its annex(es) and appendix.

London, 19 February 2010

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

ANNEX I

THE MEASURES AND TIMELINES OF THE AGREED PAEDIATRIC INVESTIGATION PLAN AND THE SUBSET(S) OF THE PAEDIATRIC POPULATION AND CONDITION(S) COVERED BY THE WAIVER

A. CONDITION(S)

Type I diabetes mellitus
Type II diabetes mellitus

B. WAIVER

- **Condition**

  Type I diabetes mellitus

  The waiver applies to:

  – Neonates and infants from birth to less than 12 months of age;

  – for Insulin degludec, 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.

- **Condition**

  Type II diabetes mellitus

  The waiver applies to:

  – Children from birth to less than 10 years of age;

  – for Insulin degludec, 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.

C. PAEDIATRIC INVESTIGATION PLAN

C.1

- **Condition to be investigated**

  Type I diabetes mellitus

- **Proposed PIP indication**

  Treatment of type I diabetes mellitus

- **Subset(s) of the paediatric population concerned by the paediatric development**

  From 1 to less than 18 years.

- **Formulation(s)**

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

- **Studies**

Area	Number of studies	Description
Quality	1	1) Availability of a dispensing system capable of delivering insulin doses in 0.5 U steps.
Non-clinical		Not applicable.
Clinical	4	2) Randomised, single-centre, double-blind, two-period cross-over, single-dose trial investigating the pharmacokinetic properties of Insulin degludec and insulin glargine in children from 6 to less than 18 years of age (and in adults) with type I diabetes mellitus. 3) Randomised, open-label, parallel-group, 6-month efficacy and safety non-inferiority study of Insulin degludec 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. 4) PK/PD modelling study in children from 1 to less than 18 years of age, with type I diabetes mellitus. 5) Bioequivalence study in adults of insulin 454 drug substance manufactured for phase 2 with *S. cerevisiae* strain MT748 and insulin 454 drug substance manufactured for phase 3 with *S. cerevisiae* strain NN729.

C.2

- **Condition to be investigated**

  Type II diabetes mellitus

- **Proposed PIP indication**

  Treatment of type II diabetes mellitus

- **Subset(s) of the paediatric population concerned by the paediatric development**

  From 10 to less than 18 years.

- **Formulation(s)**

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

- **Studies**

Area	Number of studies	Description
Quality	1	1) Availability of a dispensing system capable of delivering insulin doses in 0.5 U steps.
Non-clinical		Not applicable.
Clinical	5	2) Randomised, single-centre, double-blind, two-period cross-over, single-dose trial investigating the pharmacokinetic properties of Insulin degludec 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) 3) Randomised, open-label, parallel-group, 6-month efficacy and safety non-inferiority study of Insulin degludec 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) 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) 5) Bioequivalence study in adults of insulin 454 drug substance manufactured for phase 2 with *S. cerevisiae* strain MT748 and insulin 454 drug substance manufactured for phase 3 with *S. cerevisiae* strain NN729. (same as for condition 1) 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.

Measures to address long term follow-up of potential safety or efficacy issues in relation to paediatric use:	**No**
Date of completion of the paediatric investigation plan:	**By July 2013**
Deferral for some or all studies contained in the paediatric investigation plan:	**Yes**