EMA/662328/2017

European Medicines Agency decision

P/0325/2017

of 31 October 2017

on the acceptance of a modification of an agreed paediatric investigation plan for recombinant parathyroid hormone (Natpar), (EMEA-001526-PIP01-13-M02) 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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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 European Medicines Agency's decision P/0205/2014 issued on 8 August 2014 and the decision P/0255/2015 issued on 30 October 2015,

Having regard to the application submitted by Shire Pharmaceuticals Ireland Limited on 26 June 2017 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 September 2017, 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 recombinant parathyroid hormone (Natpar), powder and solvent for 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 Shire Pharmaceuticals Ireland Limited, 5 Riverwalk, Citywest Business Campus, Dublin 24, Ireland.

EMA/PDCO/428715/2017
London, 15 September 2017

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

EMEA-001526-PIP01-13-M02

Scope of the application

Active substance(s):

Recombinant parathyroid hormone

Invented name:

Natpar

Condition(s):

Treatment of hypoparathyroidism

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder and solvent for solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Shire Pharmaceuticals Ireland Limited

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Shire Pharmaceuticals Ireland Limited submitted to the European Medicines Agency on 26 June 2017 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0205/2014 issued on 8 August 2014 and the decision P/0255/2015 issued on 30 October 2015.

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

The procedure started on 18 July 2017.

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 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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of hypoparathyroidism

2.1.1. Indication(s) targeted by the PIP

Long-term treatment of subjects with hypoparathyroidism

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder and solvent for solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of lower strength of existing dose form and age-appropriate delivery device for use in children from birth to less than 12 years of age
Non-clinical studies	1	**Study 2** Repeat-dose toxicity study in juvenile rats, including bone densitometry, histomorphometry and histopathology, plus femur and tibia length
Clinical studies	4	**Study 3** Open-label, non-controlled PK/PD trial to evaluate the mean baseline corrected change in serum total calcium concentrations and plasma PTH(1-84) concentrations after single dose subcutaneous injection of recombinant parathyroid hormone(rhPTH(1-84)) and after 2 subcutaneous injections of rhPTH(1-84) given 12 hours apart (if supported by PIP Study 7, Stage 2) in children from 12 to less than 18 years of age with hypoparathyroidism

		Study 4 Open-label, non-controlled PK/PD trial to evaluate the mean baseline corrected change in serum total calcium concentrations and plasma PTH (1-84) concentrations after single dose subcutaneous injection of recombinant parathyroid hormone and after 2 subcutaneous injections of rhPTH(1-84) given 12 hours apart (if supported by PIP Study 7, Stage 2) in children from birth to less than 12 years of age with hypoparathyroidism **Study 5** Open-label, non-controlled trial to assess safety and activity of recombinant parathyroid hormone, administered with multiple-dose pen injection device as add-on to best standard of care in children from 12 to less than 18 years of age with hypoparathyroidism **Study 6** Open-label, non-controlled trial to assess safety and activity of recombinant parathyroid hormone, administered with age-appropriate delivery device as add-on to best standard of care in children from birth to less than 12 years of age with hypoparathyroidism
Extrapolation, modelling and simulation studies	1	**Study 7** Development of a population PK model and quantitative system pharmacology model (QSP) to perform simulations and to support the choice of doses for the studies in children from birth to less than 18 years of age
Other studies	0	Not applicable
Other measures	0	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 September 2023
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 hypoparathyroidism

Authorised indication(s):

Natpar is indicated as adjunctive treatment of adult patients with chronic hypoparathyroidism who cannot be adequately controlled with standard therapy alone.

Authorised pharmaceutical form(s):

Powder and solvent for solution for injection

Authorised route(s) of administration:

Subcutaneous use