EMA/473174/2013

European Medicines Agency decision

P/0188/2013

of 8 August 2013

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for naltrexone (hydrochloride) / bupropion (hydrochloride) (EMEA-001373-PIP01-12) 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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An agency of the European Union

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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 application submitted by Orexigen Therapeutics, Inc. on 5 November 2012 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 July 2013, 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 naltrexone (hydrochloride) / bupropion (hydrochloride), prolonged-release tablet, oral 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 naltrexone (hydrochloride) / bupropion (hydrochloride), prolonged-release tablet, oral 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 naltrexone (hydrochloride) / bupropion (hydrochloride), prolonged-release tablet, oral 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 Orexigen Therapeutics, Inc., 3344 North Torrey Pines Ct., Suite 200 92037 - La Jolla, United States.

Done at London, 8 August 2013

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

EMA/PDCO/307717/2013

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001373-PIP01-12

Scope of the application

Active substance(s):

Naltrexone (hydrochloride) / bupropion (hydrochloride)

Condition:

Treatment of obesity

Pharmaceutical form:

Prolonged-release tablet

Route of administration:

Oral use

Name/corporate name of the PIP applicant:

Orexigen Therapeutics, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Orexigen Therapeutics, Inc. submitted for agreement to the European Medicines Agency on 5 November 2012 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 12 December 2012.

Supplementary information was provided by the applicant on 25 April 2013.

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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)(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, 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.

   The Norwegian Paediatric Committee member agrees 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 European Medicines Agency, together with its annex and appendix.

London, 19 July 2013

On behalf of the Paediatric Committee
Dr Daniel Brasseur, 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 obesity

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- for prolonged-release tablet, for oral use;
- on the grounds that the condition for which the specific medicinal product is intended does not occur in the specified paediatric subsets

and to:

- the paediatric population from 2 to less than 6 years of age;
- for prolonged-release tablet, for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition: treatment of obesity

2.1.1. Indication targeted by the PIP

Treatment of obesity.

2.1.2. Subsets of the paediatric population concerned by the paediatric development

From 6 to less than 18 years of age.

2.1.3. Pharmaceutical form

Prolonged-release tablet.

2.1.4. Measures

Area	Number of measures	Description
Quality	1	**Measure 1:** Development of an age-appropriate oral preparation solid form, for oral use in children from 6 to less than 12 years of age
Non-clinical	2	**Measure 2:** Pubertal mice toxicity study to assess toxicokinetics, CNS parameters, learning, memory, behaviour, and sexual maturation **Measure 3:**

Area	Number of measures	Description
		Pre-pubertal mice toxicity study to assess CNS development, learning, memory, behaviour and sexual maturation
Clinical	4	**Measure 4:** Double-blind, randomised, multicentre, placebo-controlled, multiple dose study to assess pharmacokinetics, pharmacodynamics and tolerability of naltrexone and bupropion as fixed-dose combination, in post-pubertal obese adolescents from 12 to less than 18 years of age **Measure 5:** Double-blind, randomised, multi-centre, placebo-controlled study to assess safety and efficacy of naltrexone and bupropion as fixed-dose combination, in post-pubertal obese adolescents from 12 to less than 18 years of age **Measure 6:** Double-blind, randomised, multicentre, placebo-controlled, multiple dose study to assess pharmacokinetics, pharmacodynamics and tolerability of naltrexone and bupropion as fixed-dose combination, in pre-pubertal obese children from 6 to less than 12 years of age **Measure 7:** Double-blind, randomised, multi-centre, placebo-controlled study to assess safety and efficacy of naltrexone and bupropion as fixed-dose combination, in pre-pubertal obese children from 6 to less than 12 years of age

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By January 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes