EMA/762883/2017

European Medicines Agency decision

P/0365/2017

of 1 December 2017

on the acceptance of a modification of an agreed paediatric investigation plan for naltrexone (hydrochloride) / bupropion (hydrochloride) (Mysimba), (EMEA-001373-PIP01-12-M03) 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/0188/2013 issued on 8 August 2013, the decision P/0071/2016 issued on 18 March 2016 and the decision P/0332/2016 issued on 2 December 2016,

Having regard to the application submitted by Orexigen Therapeutics Ireland Limited on 21 July 2017 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 13 October 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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 naltrexone (hydrochloride) / bupropion (hydrochloride) (Mysimba), prolonged-release tablet, oral use, 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 Orexigen Therapeutics Ireland Limited, 2nd Floor Palmerston House, Fenian Street, D02 WD37 - Dublin, Ireland.

EMA/PDCO/490523/2017
London, 13 October 2017

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

EMEA-001373-PIP01-12-M03

Scope of the application

Active substance(s):

Naltrexone (hydrochloride) / bupropion (hydrochloride)

Invented name:

Mysimba

Condition(s):

Treatment of obesity

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Prolonged-release tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Orexigen Therapeutics 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, Orexigen Therapeutics Ireland Limited submitted to the European Medicines Agency on 21 July 2017 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/0188/2013 issued on 8 August 2013, the decision P/0071/2016 issued on 18 March 2016 and the decision P/0332/2016 issued on 2 December 2016.

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

The procedure started on 15 August 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 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.

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

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, 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, 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	1	***Measure 2*** Mice juvenile toxicity study to assess toxicokinetics, CNS parameters, learning, memory, behaviour, and sexual maturation.

		Measure 3 Removed in procedure EMEA-001373-PIP01-12-M01.
Clinical	4	***Measure 4*** Randomized, open-label, single-dose pharmacokinetic and safety study of naltrexone and bupropion extended-release fixed-dose combination in 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 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.
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

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

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s)

1. Treatment of obesity

Authorised indication:

- management of weight in adult patients (≥18 years) with an initial Body Mass Index (BMI) of
  - ≥ 30 kg/m2 (obese), or
  - ≥ 27 kg/m2 to < 30 kg/m2 (overweight) in the presence of one or more weight-related co-morbidities (e.g., type 2 diabetes, dyslipidaemia, or controlled hypertension)

Treatment with Mysimba should be discontinued after 16 weeks if patients have not lost at least 5% of their initial body weight.

Authorised pharmaceutical form(s)

Prolonged-release tablet

Blue, biconvex, round tablet of 11.9 mm diameter debossed with “NB-890” on one side

Authorised route(s) of administration

Oral use