EMA/391701/2014

European Medicines Agency decision

P/0239/2014

of 22 September 2014

on the acceptance of a modification of an agreed paediatric investigation plan for vortioxetine (Brintellix), (EMEA-000455-PIP02-10-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/130/2011 issued on 8 June 2011, and the decision P/282/11 issued on 29 November 2011,

Having regard to the application submitted by H. Lundbeck A/S on 28 March 2014 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 12 September 2014, 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) Regulation (EC) No 1901/2006, 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 vortioxetine (Brintellix), film-coated tablet, age appropriate oral liquid dosage form, oral 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 H. Lundbeck A/S, Ottiliavej 9, 2500 – Valby, Denmark.

Done at London, 22 September 2014

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

EMA/PDCO/465905/2014 Corr.

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan (after re-examination)

EMEA-000455-PIP02-10-M02

Scope of the application

Active substance(s):

Vortioxetine

Invented name:

Brintellix

Condition(s):

Treatment of major depressive disorder

Treatment of generalised anxiety disorder

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Age appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

H. Lundbeck A/S

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, H. Lundbeck A/S submitted to the European Medicines Agency on 28 March 2014 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/130/2011 issued on 8 June 2011, and the decision P/282/11 issued on 29 November 2011.

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

An Opinion was adopted by the Paediatric Committee on 20 June 2014 for the above mentioned product. H. Lundbeck A/S received the Paediatric Committee Opinion on 30 June 2014.

On 25 July 2014 H. Lundbeck A/S submitted to the European Medicines Agency a written request including detailed grounds for a re-examination of the Opinion.

The re-examination procedure started on 15 August 2014.

A meeting with the Paediatric Committee took place on 11 September 2014.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report :

1.1. to revise its opinion and

- to agree to the changes regarding the measures and the timelines of the paediatric investigation plan and the timelines of the deferral in the scope set out in the Annex I of this opinion.

1.2. following re-examination, to amend the scope of the modifications of the paediatric investigation plan.

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 European Medicines Agency, together with its annexes and appendix.

London, 12 September 2014

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 major depressive disorder

The waiver applies to:

- All subsets of the paediatric population from birth to less than 24 months of age;
- for film-coated tablets for oral use and age appropriate oral liquid dosage form;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset.

The waiver applies to:

- All subsets of the paediatric population from 24 months to less than 7 years of age;
- for film-coated tablets for oral use and age appropriate oral liquid dosage form;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible in the specified paediatric subset.

1.2. Condition

Treatment of generalised anxiety disorder

The waiver applies to:

- All subsets of the paediatric population from birth to less than 7 years of age;
- for film-coated tablets for oral use and age appropriate oral liquid dosage form;
- 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 major depressive disorder

2.1.1. Indication(s) targeted by the PIP

Treatment of major depressive disorder

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

From 7 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age appropriate oral liquid dosage form

2.1.4. Studies

Area	Number of studies	Description
Quality	1	**Study 1:** Development of age-appropriate liquid formulation for oral use.
Non-clinical	3	**Study 2:** Toxicokinetic study in juvenile animals. **Study 3:** Dose-range finding study in juvenile animals. **Study 4:** Toxicity study in juvenile animals.
Clinical	5	**Study 5:** Open-label study to assess the pharmacokinetics and tolerability of multiple oral dosing of vortioxetine in children and adolescent patients with a DSM-IV diagnosis of depressive or anxiety disorder (12708A). **Study 6:** Two-phase, single- and double-blind, randomised, placebo-controlled, multicentre, short-term study of vortioxetine and fluoxetine in paediatric patients with major depressive disorder (MDD) from 7 to less than 12 years of age (12709A). **Study 7:** Double-blind, randomised, placebo-controlled and active comparator, 3 arm, multicentre, short-term study of vortioxetine and fluoxetine in paediatric patients with major depressive disorder (MDD) from 12 to less than 18 years of age (12710A). **Study 8:** Double-blind, randomised, placebo-controlled, multicentre, relapse-prevention study of vortioxetine in paediatric patients with major depressive disorder (MDD) from 7 to less than 18 years of age (13546A). **Study 9:** Long-term, open-label, flexible-dose, extension study of vortioxetine in paediatric patients with major depressive disorder (MDD) from 7 to less than 18 years of age (12712A).

2.2. Condition

Treatment of generalised anxiety disorder

2.2.1. Indication(s) targeted by the PIP

Treatment of generalised anxiety disorder

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

From 7 to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Age appropriate oral liquid dosage form

2.2.4. Studies

Area	Number of studies	Description
Quality	1	**Study 1:** Same study as for major depressive disorder.
Non-clinical	3	**Studies 2, 3, 4:** Same studies as for major depressive disorder.
Clinical	4	**Study 5:** Same study as for major depressive disorder. **Study 10:** Double-blind, randomised, placebo-controlled, multicentre, short-term efficacy study of vortioxetine in paediatric patients with generalised anxiety disorder (GAD) from 7 to less than 18 years of age (12711A). **Study 11:** Double-blind, randomised, placebo-controlled, multicentre, relapse - prevention study with vortioxetine in paediatric patients with generalised anxiety disorder (GAD) from 7 to less than 18 years of age (13547A). **Study 12:** Long-term, open-label, extension, flexible-dose, safety study of vortioxetine in paediatric patients with generalised anxiety disorder (GAD) from 7 to less than 18 years of age (13996A).

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By January 2022
Deferral for one or more studies contained in the paediatric investigation plan:	Yes