EMA/201276/2013

European Medicines Agency decision

P/0110/2013

of 30 April 2013

on the agreement of a paediatric investigation plan and on the granting of a waiver for bumetanide (EMEA-001303-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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on the agreement of a paediatric investigation plan and on the granting of a waiver for bumetanide (EMEA-001303-PIP01-12) 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 Neurochlore on 4 June 2012 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 March 2013, in accordance with Article 18 of Regulation (EC) No 1901/2006, 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 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 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 bumetanide, age-appropriate oral liquid formulation, 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 waiver for bumetanide, age-appropriate oral liquid formulation, 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

This decision is addressed to Neurochlore, INMED, parc scientifique de Luminy, 13173 Marseille cedex 09, France.

Done at London, 30 April 2013

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

EMA/PDCO/819342/2012

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

EMEA-001303-PIP01-12

Scope of the application

Active substance(s):

Bumetanide

Condition(s):

Treatment of autistic spectrum disorder

Pharmaceutical form(s):

Age-appropriate oral liquid formulation

Prolonged-release tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Neurochlore

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Neurochlore submitted for agreement to the European Medicines Agency on 4 June 2012 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 11 July 2012.

Supplementary information was provided by the applicant on 17 December 2012.

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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 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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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, 15 March 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 autistic spectrum disorder

The waiver applies to:

- The paediatric population from birth to less than 2 years;
- for oral liquid, prolonged-release tablet, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of Autistic Spectrum Disorder (ASD)

2.1.1. Indication(s) targeted by the PIP

Treatment of communication and social skills associated with autistic spectrum disorder.

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

From 2 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

For age-appropriate oral liquid formulation, prolonged-release tablet, oral use.

2.1.4. Measures

Area	Number of measures	Description
Quality	2	Measure 1: Development of prolonged-release minitablets Measure 2: Development of age-appropriate oral liquid formulation
Non-clinical	1	Measure 3: Genotoxicity: In vitro mammalian chromosome aberration test in L5178Y Mouse Lymphoma Cells TK+/-.
Clinical	4	Measure 4: (NeuroClin02) multicentre, randomised, double-blind, placebo-controlled, dose finding study to evaluate the pharmacokinetic and efficacy of Bumetanide in children from 2 years to less than 18 years with ASD. Measure 5: (Neuro-001ASD (NeuroClin03)) 6-month, double-blind, randomized, placebo-controlled trial to evaluate safety and efficacy, of Bumetanide in children from 2 years to less than 18 years with ASD, followed by an open label 6-month period and a 6-week discontinuation phase. Measure 6: (Neuro-002ASD (NeuroClin04)) randomized, double-blind, placebo-controlled study to evaluate the efficacy of Bumetanide minitablets in children from 8 years to less than 18 years.

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 December 2016
Deferral for one or more measures contained in the paediatric investigation plan:	No