EMA/12333/2017

European Medicines Agency decision

P/0016/2017

of 31 January 2017

on the refusal of a modification of an agreed paediatric investigation plan for bumetanide, (EMEA-001303-PIP01-12-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0110/2013 issued on 30 April 2013,

Having regard to the application submitted by Neurochlore on 26 September 2016 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 December 2016, 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 refusal of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the refusal 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 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, are hereby refused.

Article 2

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

EMA/PDCO/655978/2016
London, 16 December 2016

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

EMEA-001303-PIP01-12-M01

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 22 of Regulation (EC) No 1901/2006 as amended, Neurochlore submitted to the European Medicines Agency on 26 September 2016 an application for modification of the agreed paediatric investigation plan with a waiver as set out in the European Medicines Agency's decision P/0110/2013 issued on 30 April 2013.

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

The procedure started on 18 October 2016.

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 refuse the changes proposed by the applicant regarding the paediatric investigation plan.

   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 remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex 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

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)

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	3	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