EMA/193109/2021

European Medicines Agency decision

P/0170/2021

of 9 April 2021

on the acceptance of a modification of an agreed paediatric investigation plan for bumetanide (EMEA-001303-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/0110/2013 issued on 30 April 2013, the decision P/0016/2017 issued on 31 January 2017 and the decision P/0340/2017 issued on 10 November 2017,

Having regard to the application submitted by Les Laboratoires Servier on 17 December 2020 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 26 March 2021, 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 bumetanide, age-appropriate oral liquid formulation, 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 Les Laboratoires Servier, 50, rue Carnot, 92284 - Suresnes Cede, France.

EMA/PDCO/51214/2021
Amsterdam, 26 March 2021

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

EMEA-001303-PIP01-12-M03

Scope of the application

Active substance(s):

Bumetanide

Condition(s):

Treatment of autistic spectrum disorder

Pharmaceutical form(s):

Age-appropriate oral liquid formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Les Laboratoires Servier

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Les Laboratoires Servier submitted to the European Medicines Agency on 17 December 2020 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 decision P/0016/2017 issued on 31 January 2017 and the decision P/0340/2017 issued on 10 November 2017.

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

The procedure started on 26 January 2021.

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.

   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 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 (PIP)

1. Waiver

1.1. Condition

Treatment of autistic spectrum disorder

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- age-appropriate oral liquid formulation, 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

2.1.1. Indication(s) targeted by the PIP

Treatment of core symptoms of autism spectrum disorder (ASD) in children and adolescents from 2 to 18 years of age

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

2.1.4. Measures

Area	Number of measures	Description
Quality	1	*Study 1* *Deleted in procedure EMEA-001303-PIP01-12-M02* **Study 2** Development of age-appropriate oral liquid formulation.
Non-clinical	1	**Study 3** (NeuroTox02) Genotoxicity: In vitro mammalian chromosome aberration test in L5178Y Mouse Lymphoma Cells TK+/-.

Clinical	3	**Study 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 of age with ASD. **Study 5** (CL3-95008-001) A 6-month, double-blind, randomized, placebo-controlled trial to evaluate safety and efficacy of Bumetanide in children and adolescents from 7 years to less than 18 years of age with autistic spectrum disorder (ASD), followed by an open label 6-month period and a 6-week discontinuation phase. *Study 6* *Deleted in procedure EMEA-001303-PIP01-12-M02* **Study 7** (CL3-95008-002) A 6-month, double-blind, randomized, placebo-controlled trial to evaluate safety and efficacy of Bumetanide in children from 2 years to less than 7 years of age with autistic spectrum disorder (ASD), followed by an open label 6-month period and a 6-week discontinuation phase.

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 September 2022
Deferral for one or more measures contained in the paediatric investigation plan:	No