EMA/369864/2019

European Medicines Agency decision

P/0247/2019

of 16 July 2019

on the acceptance of a modification of an agreed paediatric investigation plan for balovaptan (EMEA-001918-PIP01-15-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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on the acceptance of a modification of an agreed paediatric investigation plan for balovaptan (EMEA-001918-PIP01-15-M02) 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 European Medicines Agency's decision P/0073/2017 issued on 17 March 2017 and the decision P/0259/2018 issued on 15 August 2018,

Having regard to the application submitted by Roche Registration GmbH on 20 February 2019 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 29 May 2019, 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 balovaptan, dispersible 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 Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/205355/2019
Amsterdam, 29 May 2019

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

EMEA-001918-PIP01-15-M02

Active substance(s):

Balovaptan

Condition(s):

Treatment of autism spectrum disorder

Pharmaceutical form(s):

Dispersible tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted to the European Medicines Agency on 20 February 2019 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/0073/2017 issued on 17 March 2017 and the decision P/0259/2018 issued on 15 August 2018.

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

The procedure started on 1 April 2019.

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 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 autism spectrum disorder

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- dispersible tablet, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition

Treatment of autism spectrum disorder

2.1.1. Indication(s) targeted by the PIP

Treatment of core social and communication deficits in people with autism spectrum disorder aged 2 years or older

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)

Dispersible tablet, oral use

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	3	**Study 1** Development of a small dispersible tablet for use in children between 2 and 18 years of age **Study 2** Compatibility study of the tablet formulation in the presence of specified liquids (tap water, apple juice, orange juice) **Study 3** Dose recovery to determine minimum volume for dispersion and rinsing for dosing accuracy of the final selected doses of

		the tablet formulation
Non-clinical studies	2	**Study 4** Oral (gavage) toxicity study in the juvenile rat with a 90 day treatment-free period **Study 5** 26-week toxicity study in juvenile rats
Clinical studies	3	**Study 6** PK, safety and efficacy study in children and adolescents with Autism spectrum disorder from 5 to less than 18 years of age (BP30153) **Study 7** Efficacy and safety study in children and adolescents with Autistic Spectrum Disorder, from 5 to less than 18 years old (P3STUD2) **Study 8** PK, efficacy and safety study in children with Autism spectrum disorder from 2 to less than 5 years old (P3STUD3)
Extrapolation, modelling and simulation studies	3	**Study 9** Modelling and simulation study1: balovaptan physiologically-based pharmacokinetic (PBPK) modelling for dose selection for studies BP30153, P3STUD2 and P3STUD3 **Study 10** Modelling and simulation study 2: balovaptan population pharmacokinetic (PopPK) modelling to characterise PK in adult and paediatric patients with ASD and for dose selection for P3STUD2 and P3STUD3 **Study 11** Modelling and simulation study 3: balovaptan population pharmacokinetic/pharmacodynamic (PopPK/PD) modelling of relationship between balovaptan exposure and efficacy responses and/or safety parameters to support dose selection for P3STUD2 and P3STUD3
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2029
Deferral for one or more measures contained in the paediatric investigation plan:	Yes