EMA/137097/2017

European Medicines Agency decision

P/0073/2017

of 17 March 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for 8-chloro-5-methyl-1-[trans-4-(pyridin-2-yloxy)cyclohexyl]-5,6-dihydro-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine (RO5285119) (EMEA-001918-PIP01-15) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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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 application submitted by Roche Registration Ltd on 22 January 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 27 January 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation 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 deferral 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 deferral.

(4) 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 8-chloro-5-methyl-1-[trans-4-(pyridin-2-yloxy)cyclohexyl]-5,6-dihydro-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine (RO5285119), dispersible 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 deferral for 8-chloro-5-methyl-1-[trans-4-(pyridin-2-yloxy)cyclohexyl]-5,6-dihydro-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine (RO5285119), dispersible 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

A waiver for 8-chloro-5-methyl-1-[trans-4-(pyridin-2-yloxy)cyclohexyl]-5,6-dihydro-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine (RO5285119), dispersible 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 4

This decision is addressed to Roche Registration Ltd, 6 Falcon Way, Shire Park, AL7 1TW - Welwyn Garden City, United Kingdom.

EMA/PDCO/739930/2016
London, 27 January 2017

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

EMEA-001918-PIP01-15

Scope of the application

Active substance(s):

8-chloro-5-methyl-1-[trans-4-(pyridin-2-yloxy)cyclohexyl]-5,6-dihydro-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine (RO5285119)

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 Ltd

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Roche Registration Ltd submitted for agreement to the European Medicines Agency on 22 January 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 1 March 2016.

Supplementary information was provided by the applicant on 4 November 2016. The applicant proposed modifications to the paediatric investigation plan.

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 deferral in accordance with Article 21 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)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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.

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 table, 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: RO5285119 physiologically-based pharmacokinetic (PBPK) modelling for dose selection for studies BP30153, P3STUD2 and P3STUD3. **Study 10** Modelling and simulation study 2: RO5285119 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: RO5285119 population pharmacokinetic/pharmacodynamic (PopPK/PD) modelling of relationship between RO5285119 exposure and efficacy responses and/or safety parameters to support dose selection for P3STUD2 and P3STUD3.
Other studies		Not applicable.
Other measures		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