EMA/160752/2015

European Medicines Agency decision

P/0075/2015

of 1 April 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for a derivative of 2-methyl-6-(5-methyl-3-phenyl-isoxazol-4-ylmethoxy)-pyridine (RG1662) (EMEA-001506-PIP02-14) 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 application submitted by Roche Registration Ltd on 12 May 2014 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 13 February 2015, 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 a derivative of 2-methyl-6-(5-methyl-3-phenyl-isoxazol-4-ylmethoxy)-pyridine (RG1662), tablet, granules, 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 a derivative of 2-methyl-6-(5-methyl-3-phenyl-isoxazol-4-ylmethoxy)-pyridine (RG1662), tablet, granules, 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 a derivative of 2-methyl-6-(5-methyl-3-phenyl-isoxazol-4-ylmethoxy)-pyridine (RG1662), tablet, granules, 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.

Done at London, 1 April 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/754667/2014

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

EMEA-001506-PIP02-14

Scope of the application

Active substance(s):

A derivative of 2-methyl-6-(5-methyl-3-phenyl-isoxazol-4-ylmethoxy)-pyridine (RG1662)

Condition(s):

Treatment of Down syndrome

Pharmaceutical form(s):

Tablet

Granules

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 12 May 2014 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 18 June 2014.

Supplementary information was provided by the applicant on 24 November 2014. The applicant proposed modifications to the paediatric investigation plan.

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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 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)(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, 13 February 2015

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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 (PIP)

1. Waiver

1.1. Condition

Treatment of Down syndrome

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- tablet, granules, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of Down syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of intellectual disability associated with Down syndrome

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)

Tablet

Granules

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	4	**Study 1** Technical feasibility validation of the sachet filling step of granules manufacturing. **Study 2** Dose recovery study of the granule formulation. **Study 3** Compatibility study of the fine granule formulation with food. **Study 4** Palatability (taste and acceptability) testing of the granule formulation as part of a clinical pharmacology study in healthy adult volunteers (Study WP28978).

Non-clinical studies	1	**Study 5** Definitive juvenile toxicity study (9000198).
Clinical studies	5	**Study 6** Randomised, double-blind, placebo controlled, multicentre trial, 2 doses design to assess the efficacy, safety and tolerability of RG1662, and validity of pharmacokinetic model predictions of dose selection in adolescents (BP27832). **Study 7** Randomised, double-blind, placebo-controlled, parallel group study to explore the pharmacokinetics, pharmacodynamic effects, efficacy, safety and tolerability of RG1662 compared with placebo in children with Down syndrome aged from 6 to less than 12 years of age (WP28760). **Study 8** Double-blind, placebo-controlled, randomised, multicentre long-term efficacy and safety study of RG1662 as monotherapy in adolescents with Down syndrome aged from 12 to less than 18 years of age (and adults) (P3STUD1). **Study 9** Double-blind, placebo-controlled, randomised, multicentre long-term efficacy and safety study of RG1662 as monotherapy in children with Down syndrome aged from 6 to less than 12 years of age (P3STUD2). **Study 10** Double-blind, placebo-controlled, randomised, multicentre long-term efficacy and safety study of RG1662 as monotherapy in children with Down syndrome aged from 2 to less than 6 years of age (P3STUD3).
Extrapolation, modelling and simulation studies	3	**Study 11** Physiologically based pharmacokinetic (PBPK) model. **Study 12** Population pharmacokinetic (PopPK) model. **Study 13** Population pharmacokinetic/pharmacodynamic (PopPK/PD) model.
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:	No
Date of completion of the paediatric investigation plan:	By December 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes