EMA/203225/2013

European Medicines Agency decision

P/0107/2013

of 30 April 2013

on the acceptance of a modification of an agreed paediatric investigation plan for (3aR,4S,7aR)-Octahydro-4-hydroxy-4-[(3-methylphenyl)ethynyl]-1H-indole-1-carboxylic acid methyl ester (EMEA-001003-PIP01-10-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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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/152/2011 issued on 30 June 2011 and the decision P/0126/2012 issued on 4 July 2012,

Having regard to the application submitted by Novartis Europharm Ltd on 11 December 2012 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 March 2013, 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 (3aR,4S,7aR)-Octahydro-4-hydroxy-4-[(3-methylphenyl)ethynyl]-1H-indole-1-carboxylic acid methyl ester, capsule, hard, powder for oral suspension, 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 Novartis Europharm Ltd, Wimblehurst Road, West Sussex, RH12 5AB Horsham, United Kingdom.

Done at London, 30 April 2013

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/102840/2013

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

EMEA-001003-PIP01-10-M02

Scope of the application

Active substance(s):

(3aR,4S,7aR)-Octahydro-4-hydroxy-4-[(3-methylphenyl)ethynyl]-1H-indole-1-carboxylic acid methyl ester

Condition(s):

Treatment of Fragile X syndrome

Pharmaceutical form(s):

Capsule, hard

Powder for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Ltd

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Ltd submitted to the European Medicines Agency on 11 December 2012 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/152/2011 issued on 30 June 2011 and the decision P/0126/2012 issued on 4 July 2012.

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

The procedure started on 16 January 2013.

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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 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, 15 March 2013

On behalf of the Paediatric Committee
Dr Daniel Brasseur, 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

1. Waiver

Not applicable.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of Fragile X syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of behavioural symptoms of Fragile X syndrome.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Capsule, hard.

Powder for oral suspension.

2.1.4. Measures

Area	Number of measures	Description
Quality	1	Measure 1 Development of age-appropriate powder for oral suspension formulation(s).
Non-clinical	5	Measure 2 4-week oral (gavage) toxicity study including a dose-titration phase in dogs. Measure 3 52-week oral gavage toxicity study in the Beagle dog with 4 weeks recovery. Measure 4 13-week oral (gavage) investigative toxicity study in rat. Measure 5 A modified oral pre and postnatal study of AFQ056 in the rat. Measure 6 Juvenile rat study.
Clinical	11	Measure 7 Sequential, open-label, two-period study to assess the pharmacokinetics, safety and tolerability of two dose levels of AFQ056 in male, adolescent patients with Fragile X Syndrome (FXS).

Area	Number of measures	Description
		Measure 8 Randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy, safety and tolerability of AFQ056 in adolescent (12-17 years of age) patients with FXS. Measure 9 Sequential, open-label, two-period study to assess the pharmacokinetics, safety and tolerability of single and multiple doses of AFQ056 in patients with FXS aged 5-11 years. Measure 10 Randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy, safety and tolerability of AFQ056 in paediatric (5-11 years of age) patients with FXS. Measure 11 Randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy of AFQ056 in adolescent (12-17 years of age) patients with FXS over 12 months of treatment. Measure 12 Open-label, flexible-dose, long-term safety study in FXS patients who have completed the AFQ056 core study CAFQ056B2214, or the PK study CAFQ056B2131. Measure 13 Randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy of AFQ056 in paediatric (5-11 years of age) patients with FXS over 12 months of treatment. Measure 14 Open-label, flexible dose, long-term safety study in children with FXS who have completed the AFQ056 core study CAFQ056B2215 or the PK study CAFQ056B2154. Measure 15 Randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy of AFQ056 in paediatric (0-4 years of age) patients with FXS over 12 months of treatment. Measure 16 Exploratory study to characterize the disease, to assess the feasibility of conducting studies in children less than 5 years of age and in female patients, as well as to identify potential biomarkers of disease modification. Measure 17

Area	Number of measures	Description
		Randomized, open-label, five period, crossover study to evaluate the single dose pharmacokinetics and food effect of two paediatric AFQ056 formulations in healthy adults.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By February 2021
Deferral for one or more studies contained in the paediatric investigation plan:	Yes