EMA/493240/2011

European Medicines Agency decision

P/152/2011

of 30 June 2011

on the agreement of a paediatric investigation plan and on the granting of a deferral for a derivative of octahydro-4-hydroxy-4-[phenylethynyl]-1H-indole-1-carboxylic acid ester (AFQ056) (EMEA-001003-PIP01-10) 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 Novartis Europharm Ltd on 2 July 2010 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 20 May 2011, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 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.

(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.

[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 octahydro-4-hydroxy-4-[phenylethynyl]-1H-indole-1-carboxylic acid ester (AFQ056), capsule, hard, powder for oral suspension, 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 octahydro-4-hydroxy-4-[phenylethynyl]-1H-indole-1-carboxylic acid ester (AFQ056), capsule, hard, powder for oral suspension, 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

This decision is addressed to Novartis Europharm Ltd, Wimblehurst Road, West Sussex, RH12 5AB – Horsham, United Kingdom.

Done at London, 30 June 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/PDCO/258790/2011

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

EMEA-001003-PIP01-10

Scope of the application

Active substance(s):

A derivative of octahydro-4-hydroxy-4-[phenylethynyl]-1H-indole-1-carboxylic acid ester (AFQ056)

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 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Ltd submitted for agreement to the European Medicines Agency on 2 July 2010 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 12 August 2010.

Supplementary information was provided by the applicant on 4 March 2011. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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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,

   The Icelandic and the Norwegian Paediatric Committee members agree 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(es) and appendix.

London, 20 May 2011

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. Studies

Area	Number of studies	Description
Quality	1	Measure 1: Development of age-appropriate powder for oral suspension formulation(s).
Non-clinical	5	Study 2: 4-week oral (gavage) toxicity study including a dose-titration phase in dogs. Study 3: 52-week oral gavage toxicity study in the Beagle dog with 4 weeks recovery. Study 4: 13-week oral (gavage) investigative toxicity study in rat. Study 5: A modified oral pre and postnatal study of AFQ056 in the rat. Study 6: Juvenile rat study.
Clinical	11	Study 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). Study 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. Study 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.

Area	Number of studies	Description
		Study 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. Study 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. Study 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. Study 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. Study 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. Study 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. Study 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. Study 17: 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

Measures to address long term follow-up of potential safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By July 2018
Deferral for one or more studies contained in the paediatric investigation plan:	Yes