EMA/473934/2015

European Medicines Agency decision

P/0175/2015

of 7 August 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for atrasentan (hydrochloride) (EMEA-001666-PIP01-14) 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 AbbVie, Ltd on 4 July 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 19 June 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 atrasentan (hydrochloride), age-appropriate oral liquid formulation, tablet, oral use, gastric 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 atrasentan (hydrochloride), age-appropriate oral liquid formulation, tablet, oral use, gastric 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 atrasentan (hydrochloride), age-appropriate oral liquid formulation, tablet, oral use, gastric 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 AbbVie, Ltd, Abbott House, Vanwall Road, SL6 4XE – Maidenhead, United Kingdom.

Done at London, 7 August 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/240483/2015
London, 19 June 2015

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

EMEA-001666-PIP01-14

Scope of the application

Active substance(s):

Atrasentan (hydrochloride)

Condition(s):

Treatment of nephropathy

Pharmaceutical form(s):

Age-appropriate oral liquid formulation

Tablet

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

AbbVie, Ltd

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AbbVie, Ltd submitted for agreement to the European Medicines Agency on 4 July 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 13 August 2014.

Supplementary information was provided by the applicant on 26 March 2015. The applicant proposed modifications to the paediatric investigation plan.

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A meeting with the Paediatric Committee took place on 18 June 2015.

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 nephropathy

The waiver applies to:

- the paediatric population from birth to less than 6 months;
- tablet, age-appropriate oral liquid formulation, oral use, gastric use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of nephropathy

2.1.1. Indication(s) targeted by the PIP

Treatment of multidrug-resistant nephrotic syndrome in paediatric patients

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet, age-appropriate oral liquid pharmaceutical formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral liquid formulation.
Non-clinical studies	3	**Study 2** Dose range finding study in rats. **Study 3** Postembryonic and postnatal development study in rats **Study 4** Definitive juvenile toxicity study in Sprague-Dawley rats from PND 7 to PND 90 of age.

Clinical studies	4	**Study 5** Open label, single dose escalation study to evaluate safety, tolerability and pharmacokinetics of atrasentan in patients with multidrug-resistant nephrotic syndrome aged from 6 months to onset of puberty of age. (Part 1) **Study 6** Open label multiple dose study to evaluate pharmacokinetics/pharmacodynamics, safety, and tolerability, acceptability/palatability, of atrasentan in patients with multidrug-resistant nephrotic syndrome aged from 6 months to onset of puberty. (Part 2) **Study 7** Double blind, randomised, multicentre, placebo-controlled study to evaluate safety, efficacy, tolerability, and pharmacodynamics of atrasentan in patients with multidrug-resistant nephrotic syndrome from 6 months to onset of puberty. (Part 3) **Study 8** Long-term open label extension study to evaluate safety, efficacy, and tolerability of atrasentan in patients with multidrug-resistant nephrotic syndrome aged from 6 months to onset of puberty. (Part 4)
Extrapolation, modelling and simulation studies	1	**Study 9** Atrasentan PBPK model to inform the starting dose for study 1.
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 December 2029
Deferral for one or more measures contained in the paediatric investigation plan:	Yes