EMA/900651/2018

European Medicines Agency decision

P/0034/2019

of 29 January 2019

on the acceptance of a modification of an agreed paediatric investigation plan for azilsartan medoxomil (Edarbi), (EMEA-000237-PIP01-08-M08) 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/105/2009 issued on 15 June 2009, the decision P/234/2009 issued on 27 November 2009, the decision P/106/2010 issued on 25 June 2010, the decision P/39/2011 issued on 4 February 2011, the decision P/0273/2012 issued on 21 November 2012, the decision P/0223/2013 issued on 23 September 2013 and the decision P/0210/2015 issued on 2 October 2015,

Having regard to the application submitted by Takeda Development Centre (Europe) Ltd. on 10 September 2018 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 14 December 2018, 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 azilsartan medoxomil (Edarbi), tablets, granules 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 Takeda Development Centre (Europe) Ltd., 61 Aldwych, WC2B 4AE – London, United Kingdom.

EMA/PDCO/638389/2018
London, 14 December 2018

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

EMEA-000237-PIP01-08-M08

Scope of the application

Active substance(s):

Azilsartan medoxomil

Invented name:

Edarbi

Condition(s):

Treatment of hypertension

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablets

Granules for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Takeda Development Centre (Europe) Ltd.

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Takeda Development Centre (Europe) Ltd. submitted to the European Medicines Agency on 10 September 2018 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/105/2009 issued on 15 June 2009, the decision P/234/2009 issued on 27 November 2009, the decision P/106/2010 issued on 25 June 2010, the decision P/39/2011 issued on 4 February 2011, the decision P/0273/2012 issued on 21 November 2012, the decision P/0223/2013 issued on 23 September 2013 and the decision P/0210/2015 issued on 2 October 2015.

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

The procedure started on 16 October 2018.

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 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 annexes 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 hypertension

The waiver applies to:

- preterm newborn infants, term newborn infants (from birth to less than 28 days), infants and children less than 2 years of age;
- tablets and granules for oral suspension, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition to be investigated

Treatment of hypertension

2.1.1. Indication targeted by the PIP

Treatment of essential and secondary hypertension

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

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablets

Granules for oral suspension

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of age appropriate formulation (granules for oral suspension).
Non-clinical studies	4	**Study 2** Repeat-dose range-finding toxicity study in neonatal rats. **Study 3** Repeat-dose toxicity study with recovery in neonatal rats.

		Study 4 A detailed comparative analysis of the toxicity profile of azilsartan compared to candesartan. **Study 5** Repeat dose toxicity with recovery in juvenile rats.
Clinical studies	4	**Study 6** Relative bioavailability, safety, and tolerability study in adults. **Study 7** Single-dose PK, safety, and tolerability of TAK 491 in children and adolescents. **Study 8** Randomized, double-blind, active-controlled, 6-week dose-ranging safety and efficacy study with a 2-week, randomised, double-blind, placebo-controlled withdrawal phase and 44-week open-label extension in children aged 6 years to less than 18 years with essential and secondary hypertension. **Study 9** Randomized, double-blind, 6-week dose-ranging safety and efficacy study with a 2-week randomized double-blind, placebo-controlled withdrawal phase and 2-year open-label extension in young children 2 years and older and with a weight of less than 25 kg with mild to moderate secondary hypertension.
Extrapolation, modelling and simulation studies	0	Not applicable.
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 April 2021
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s)

Treatment of hypertension

Authorised indication(s):

- treatment of essential hypertension in adults.

Authorised pharmaceutical form(s)

Tablet

Authorised route(s) of administration

Oral use