EMA/471937/2021

European Medicines Agency decision

P/0383/2021

of 8 September 2021

on the acceptance of a modification of an agreed paediatric investigation plan for tolvaptan (Samsca and associated names), (EMEA-001231-PIP02-13-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/0221/2013 issued on 9 September 2013, the decision P/0336/2014 issued on 22 December 2014, the decision P/0045/2016 issued on 26 February 2016, the decision P/0161/2016 issued on 15 June 2016, the decision P/0294/2016 issued on 4 November 2016, the decision P/0347/2017 issued on 1 December 2017, the decision P/0378/2018 issued on 7 December 2018 and the decision P/0002/2020 issued on 3 January 2020,

Having regard to the application submitted by Otsuka Pharmaceutical Netherlands B.V. on 19 April 2021 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 23 July 2021, 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 and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the 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

Changes to the agreed paediatric investigation plan for tolvaptan (Samsca and associated names), tablet, oral suspension, oral use, including changes to the deferral, 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 Otsuka Pharmaceutical Netherlands B.V., Herikerbergweg 292,1101 CT Amsterdam, The Netherlands.

EMA/PDCO/255007/2021
Amsterdam, 23 July 2021

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

EMEA-001231-PIP02-13-M08

Scope of the application

Active substance(s):

Tolvaptan

Invented name:

Samsca and associated names

Condition(s):

Treatment of dilutional hyponatraemia

Treatment of polycystic kidney disease

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Otsuka Pharmaceutical Netherlands B.V.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Otsuka Pharmaceutical Netherlands B.V. submitted to the European Medicines Agency on 19 April 2021 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/0221/2013 issued on 9 September 2013, the decision P/0336/2014 issued on 22 December 2014, the decision P/0045/2016 issued on 26 February 2016, the decision P/0161/2016 issued on 15 June 2016, the decision P/0294/2016 issued on 4 November 2016, the decision P/0347/2017 issued on 1 December 2017, the decision P/0378/2018 issued on 7 December 2018 and the decision P/0002/2020 issued on 3 January 2020.

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

The procedure started on 25 May 2021.

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 and to the deferral 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 dilutional hyponatraemia

The waiver applies to:

- preterm and term newborn infants from birth to less than 28 days of age;
- tablet, oral suspension, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

And to:

- the paediatric population from 28 days to less than 18 years of age;
- tablet, oral suspension, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

1.2. Condition

Treatment of polycystic kidney disease

The waiver applies to:

- preterm and term newborn infants from birth to less than 28 days of age;
- tablet, oral suspension, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of polycystic kidney disease

2.2. Indication(s) targeted by the PIP

Treatment of progression of autosomal dominant and of autosomal recessive polycystic kidney disease (ADPKD and ARPKD)

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

From 28 days to less than 18 years of age

2.2.2. Pharmaceutical form(s)

Tablet

Oral suspension

2.2.3. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an oral suspension for use in children younger than 4 years or who are unable to swallow tablets
Non-clinical studies	1	**Study 2** Study to evaluate the toxicity and toxicokinetics of tolvaptan in juvenile rats
Clinical studies	3	*Study 3 for condition "treatment of dilutional hyponatraemia" was deleted as a result of procedure EMEA-001231-PIP02-13-M05* *Study 4 for condition "treatment of dilutional hyponatraemia" was deleted as a result of procedure EMEA-001231-PIP02-13-M05* *Study 5 for condition "treatment of dilutional hyponatraemia" was deleted as a result of procedure EMEA-001231-PIP02-13-M05* **Study 6** Double-blind, randomised, placebo controlled trial to assess the effects of titrated oral tolvaptan on renal size, pharmacokinetics and safety in children from 4 years to less than 18 years of age diagnosed with autosomal dominant polycystic kidney disease; followed by an open label extension phase to collect additional safety and efficacy data (156-12-298) **Study 7** Open-label study to assess tolvaptan in children from 28 days to less than 12 weeks of age diagnosed with autosomal recessive polycystic kidney disease (156-12-204) **Study 8** *(This study was added as a result of procedure EMEA-001231-PIP02-13-M07)* Open-label study to assess safety and activity of tolvaptan in children from 28 days to less than 18 years of age diagnosed with autosomal recessive polycystic kidney disease
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 December 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of dilutional hyponatraemia

Authorised indication(s):

- Treatment of adult patients with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH).

2. Treatment of polycystic kidney disease

- Treatment of adult patients with chronic kidney disease (CKD) stage 1 to 4 at initiation of treatment with evidence of rapidly progressing disease to slow the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD).

Authorised pharmaceutical form(s):

Tablet

Authorised route(s) of administration:

Oral use