EMA/565789/2017

European Medicines Agency decision

P/0286/2017

of 4 October 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for 5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one (S44819) (EMEA-002057-PIP01-16) 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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on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for 5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one (S44819) (EMEA-002057-PIP01-16) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Les Laboratoires Servier on 20 October 2016 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 18 August 2017, 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 5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one (S44819), 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 5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one (S44819), 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

A waiver for 5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one (S44819), 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 4

This decision is addressed to Les Laboratoires Servier, 50, rue Carnot, 92284 - Suresnes Cedex, France.

EMA/PDCO/728557/2016
London, 18 August 2017

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

EMEA-002057-PIP01-16

Scope of the application

Active substance(s):

5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one (S44819)

Condition(s):

Treatment of ischemic stroke to improve recovery

Pharmaceutical form(s):

Powder for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Les Laboratoires Servier

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Les Laboratoires Servier submitted for agreement to the European Medicines Agency on 20 October 2016 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 29 November 2016.

Supplementary information was provided by the applicant on 29 May 2017. The applicant proposed modifications to the paediatric investigation plan.

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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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 ischemic stroke to improve recovery

The waiver applies to:

- the paediatric population from birth to less than 6 years of age;
- powder 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:

Treatment of ischemic stroke to improve recovery

2.1.1. Indication(s) targeted by the PIP

Treatment of ischemic stroke to improve recovery

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

From 6 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for oral suspension

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	3	**Study 1** Dose range-finding juvenile toxicity study in rats **Study 2** Definitive juvenile toxicity study in rats **Study 3** Evaluation of the effect of S44819 on functional recovery in a juvenile stroke model in rats.

Clinical studies	1	**Study 4** Randomised, double-blind, multicentre pharmacokinetic study of two active doses and placebo, 3 months duration and a follow-up of 9 months without treatment on top of standard of care, to assess the pharmacokinetics and to document the safety and activity of S44819 in paediatric patients from 6 to less than 18 years of age with ischaemic stroke
Extrapolation, modelling and simulation studies	2	**Study 5** Modelling and simulation study to define the initial doses of the paediatric study **Study 6** Population PK analysis of S44819 in paediatric patients with ischemic stroke
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:	No
Date of completion of the paediatric investigation plan:	By December 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes