



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/368538/2015

European Medicines Agency decision

P/0149/2015

of 10 July 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral for (4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride (SHP625) (EMA-001475-PIP02-13) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Lumena Pharmaceuticals Inc on 10 June 2013 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 22 May 2015, 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 (4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy)methyl]phenyl)methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride (SHP625), oral liquid, tablet, 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 (4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy)methyl]phenyl)methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride (SHP625), oral liquid, tablet, 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 Lumena Pharmaceuticals Inc, 12531 High Bluff Drive, Suite 110, CA 92130 - San Diego, United States.

Done at London, 10 July 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/145732/2015

London, 22 May 2015

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

EMA-001475-PIP02-13

Scope of the application

Active substance(s):

(4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride (SHP625)

Condition(s):

Treatment of Alagille syndrome

Pharmaceutical form(s):

Oral liquid

Tablet

Route(s) of administration:

Oral use

Name / corporate name of the PIP applicant:

Lumena Pharmaceuticals Inc

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Lumena Pharmaceuticals Inc submitted for agreement to the European Medicines Agency on 10 June 2013 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 17 July 2013.

Supplementary information was provided by the applicant on 2 March 2015. 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.

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 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

Not applicable.

2. Paediatric investigation plan

2.1. Condition

Treatment of Alagille syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of Alagille 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)

Oral liquid

Tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	1	Study 1: Juvenile toxicity study in rats (PND 7-21)
Clinical studies	4	Study 2: randomised double-blind, placebo controlled safety and efficacy study of SHP625 in children 12 months to 18 years with Alagille syndrome (LUM001-302) Study 3: randomised double-blind, placebo controlled safety and efficacy study of SHP625 in children 12 months to 18 years with Alagille syndrome (LUM001-301) Study 4: open label with a double-blind placebo controlled randomised drug withdrawal period, safety and efficacy study SHP625 in children 12 months to 18 years with Alagille syndrome (LUM001-304) Study 5: open label safety and tolerability study of SHP625 in children from birth to less than 12 months of age (LUM001-306)
Extrapolation, modelling and simulation studies	0	Not applicable.

Area	Number of measures	Description
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 July 2018
Deferral for one or more measures contained in the paediatric investigation plan:	Yes