EMA/145463/2022

European Medicines Agency decision

P/0097/2022

of 17 March 2022

on the acceptance of a modification of an agreed paediatric investigation plan for lisdexamfetamine (dimesylate), (Elvanse and associated names), (EMEA-000553-PIP01-09-M05) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/52/2010 issued on 9 April 2010, the decision P/122/2010 issued on 26 July 2010, the decision P/104/2011 issued on 3 May 2011, the decision P/0053/2012 issued on 23 March 2012 and the decision P/0321/2013 issued on 19 December 2013,

Having regard to the application submitted by Shire Pharmaceuticals Contracts Limited on 16 November 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 25 February 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for lisdexamfetamine (dimesylate),(Elvanse and associated names), capsules, hard, 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 Shire Pharmaceuticals Contracts Limited, Hampshire International Business Park, RG24 8 EP - Basinstoke, United Kingdom.

EMA/PDCO/709050/2021 Corr
Amsterdam, 25 February 2022

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

EMEA-000553-PIP01-09-M05

Scope of the application

Active substance(s):

Lisdexamfetamine (dimesylate)

Invented name:

Elvanse and associated names

Condition(s):

Treatment of attention deficit hyperactivity disorder

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsules, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Shire Pharmaceuticals Contracts Limited

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Shire Pharmaceuticals Contracts Limited submitted to the European Medicines Agency on 16 November 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/52/2010 issued on 9 April 2010, the decision P/122/2010 issued on 26 July 2010, the decision P/104/2011 issued on 3 May 2011 the decision P/0053/2012

issued on 23 March 2012 and the decision P/0321/2013 issued on 19 December 2013.

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

The procedure started on 4 January 2022.

Scope of the modification

Some measures 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 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)

Waiver

1.1. Condition: treatment of attention deficit hyperactivity disorder

The waiver applies to:

- The paediatric population from birth to less than 6 years of age;
- for capsules, hard; for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: treatment of attention deficit hyperactivity disorder

2.1.1. Indication(s) targeted by the PIP

Treatment of attention deficit hyperactivity disorder (ADHD)

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

From 6 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsules, hard

2.1.4. Measures

Area	**Description**
Quality	Not applicable
Non-clinical	**Study 1** 8-Week Subchronic Oral Neonatal Toxicity Study in the Sprague-Dawley Rat **Study 2** 2-Week Dose Range-Finding and 26-Week Oral Toxicity Study in the Juvenile Beagle Dog
Clinical	**Study 3** Randomized, double-blind, multicentre, parallel-group, placebo-controlled study to evaluate safety and efficacy of lisdexamfetamine dimesylate (LDX) in adolescents from 13 to less than 18 years with Attention-Deficit/Hyperactivity Disorder (ADHD)

	Study 4 Open-label, 12 months extension, multicentre study to evaluate long-term safety of lisdexamfetamine dimesylate (LDX) in adolescents aged from 13 years to less than 18 years with Attention-Deficit/Hyperactivity Disorder (ADHD) **Study 5** Randomised, double-blind, multicentre, parallel-group, placebo- and active-controlled (modified-release methylphenidate) dose-optimisation study to evaluate safety and efficacy of lisdexamfetamine dimesylate (LDX) in children aged 6 years to less than 18 years with Attention-Deficit/Hyperactivity Disorder (ADHD) **Study 6** Double-blind, placebo-controlled, randomised withdrawal, multicentre, extension, safety and efficacy study of Lisdexamfetamine Dimesylate (LDX) in children aged 6 years to less than 18 years with Attention-Deficit/Hyperactivity Disorder (ADHD) **Study 7** Double-blind, randomised, active-controlled, parallel-group study to evaluate safety and efficacy of lisdexamfetamine dimesylate compared to atomoxetine hydrochloride in children aged 6 years to less than 18 years with Attention Deficit/Hyperactivity Disorder (ADHD) **Study 8** Long-term (24 months), open-label, multicentre study to evaluate safety of lisdexamfetamine dimesylate (LDX) in children aged 6 years to less than 18 years with Attention-Deficit/Hyperactivity Disorder (ADHD)

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By October 2014
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):

Treatment of attention deficit hyperactivity disorder (ADHD)

Authorised indication(s):

Indicated as part of a comprehensive treatment programme for Attention Deficit/Hyperactivity Disorder (ADHD) in children aged 6 years and over when response to previous methylphenidate treatment is considered clinically inadequate.

Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders. Diagnosis should be made according to DSM criteria or the guidelines in ICD and should be based on a complete history and evaluation of the patient. Diagnosis cannot be made solely on the presence of one or more symptom.

The specific aetiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use of medical and specialised psychological, educational, and social resources.

A comprehensive treatment programme typically includes psychological, educational and social measures as well as pharmacotherapy and is aimed at stabilising children with a behavioural syndrome characterised by symptoms which may include chronic history of short attention span, distractibility, emotional lability, impulsivity, moderate to severe hyperactivity, minor neurological signs and abnormal EEG. Learning may or may not be impaired.

Elvanse is not indicated in all children with ADHD and the decision to use the drug must be based on a very thorough assessment of the severity and chronicity of the child's symptoms in relation to the child's age and potential for abuse, misuse or diversion.

Appropriate educational placement is essential, and psychosocial intervention is generally necessary. The use of Elvanse should always be used in this way according to the licensed indication.

Authorised pharmaceutical form(s):

Capsules, hard

Authorised route(s) of administration:

Oral use