EMA/341306/2017

European Medicines Agency decision

P/0155/2017

of 2 June 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral for mexiletine (hydrochloride), (EMEA-002012-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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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 Lupin (Europe) Ltd. on 7 July 2016 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 19 May 2017, 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.

Has adopted this decision:

Article 1

A paediatric investigation plan for mexiletine (hydrochloride), capsule, hard, oral solution, oral use, gastric 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.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Article 2

A deferral for mexiletine (hydrochloride), capsule, hard, oral solution, oral use, gastric 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 Lupin (Europe) Ltd., Victoria Court, Bexton Road, WA16 0PF - Knutsford, Cheshire, United Kingdom.

EMA/PDCO/158696/2017
London, 19 May 2017

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

EMEA-002012-PIP01-16

Scope of the application

Active substance(s):

Mexiletine (hydrochloride)

Condition(s):

Treatment of myotonic disorders

Pharmaceutical form(s):

Capsule, hard

Oral solution

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Lupin (Europe) Ltd.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Lupin (Europe) Ltd. submitted for agreement to the European Medicines Agency on 7 July 2016 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 16 August 2016.

Supplementary information was provided by the applicant on 27 February 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.

   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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of myotonic disorders

2.1.1. Indication(s) targeted by the PIP

Symptomatic treatment of myotonic disorders

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)

Capsule, hard

Oral solution

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	***Study 1*** Development of age appropriate solid formulation (capsule, not containing erythrosine as colorant) in lower strengths appropriate to the paediatric population ***Study 2*** Development of an age appropriate oral liquid formulation (oral solution)
Non-clinical studies	1	**Study 3** 11-week toxicity study in juvenile rats with a 4-week recovery period

Clinical studies	4	***Study 4*** Open-label, non-comparative study to evaluate the PK, safety and efficacy of mexiletine in children and adolescents 6 to less than 18 years of age with clinical symptoms or signs of myotonic disorders ***Study 5*** Open-label, non-comparative study to evaluate the PK, safety and efficacy of mexiletine in children 6 months to less than 6 years of age with clinical symptoms or signs of myotonic disorders ***Study 6*** Open-label, non-comparative study to evaluate the PK, safety and efficacy of mexiletine in neonates and infants less than 6 months of age with clinical symptoms or signs of myotonic disorders ***Study 7*** Open-label follow-up study evaluating the long-term safety and efficacy of mexiletine in children with myotonic disorders who have completed the initial paediatric studies
Extrapolation, modelling and simulation studies	1	***Study 8*** PK modelling study to support dosing recommendations in children
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 September 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes