EMA/517241/2018

European Medicines Agency decision

P/0287/2018

of 12 September 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for sarizotan (hydrochloride) (EMEA-001808-PIP03-17) 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 Newron Pharmaceuticals SpA on 18 December 2017 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 27 July 2018, in accordance with Article 17 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 sarizotan (hydrochloride), capsule, hard, age-appropriate oral liquid dosage form, 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 sarizotan (hydrochloride), capsule, hard, age-appropriate oral liquid dosage form, 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 sarizotan (hydrochloride), capsule, hard, age-appropriate oral liquid dosage form, 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 Newron Pharmaceuticals SpA, Via Ludovico Ariosto 21, 20091 - Bresso (Milan), Italy.

EMA/PDCO/300920/2018 Corr
London, 27 July 2018

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

EMEA-001808-PIP02-16

Scope of the application

Active substance(s):

Sarizotan (hydrochloride)

Condition(s):

Treatment of Rett syndrome

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Newron Pharmaceuticals SpA

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Newron Pharmaceuticals SpA submitted for agreement to the European Medicines Agency on 18 December 2017 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 23 January 2018.

Supplementary information was provided by the applicant on 5 May 2018. 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 17(1) 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)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 Rett syndrome

The waiver applies to:

- All subsets of the paediatric population from birth to less than 2 years of age;
- capsule, hard, oral use and age-appropriate oral liquid dosage form, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of Rett syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of respiratory abnormalities in Rett syndrome

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of lower strength of hard capsule not containing azo colorants, appropriate for the paediatric population **Study 2** Development of age-appropriate oral liquid dosage form, appropriate for the paediatric population and suitable for patients with swallowing difficulties

Non-clinical studies	3	**Study 3** Dose range-finding juvenile toxicity study to provide dose selection for the definitive juvenile non-clinical study **Study 4** Dose range-finding neonatal juvenile toxicity study to provide dose selection for the definitive juvenile non-clinical study **Study 5** Definitive juvenile toxicity study, including neurobehavioural examination (motor activity, functional observational battery, Morris maze), hormone measurements, oestrus cycle activity, seminology, reproductive assessment and detailed brain histopathology
Clinical studies	3	**Study 6** Double-blind, randomised, placebo-controlled trial to evaluate pharmacokinetics, efficacy, safety and tolerability of high and low dose of sarizotan in terms of superiority over placebo in children from 6 to less than 18 years of age (and adults) with Rett syndrome and respiratory abnormalities **Study 7** Double-blind, randomised, placebo-controlled trial to evaluate pharmacokinetics, efficacy, safety and tolerability of sarizotan in terms of superiority over placebo in children from 2 to less than 6 years of age with Rett syndrome and respiratory abnormalities **Study 8** Double-blind, randomised, placebo-controlled crossover trial to evaluate effects of sarizotan on respiratory functional parameters in children from 2 to less than 18 years of age (and adults) with Rett syndrome and respiratory abnormalities
Extrapolation, modelling and simulation studies	2	**Study 9** Modelling and simulation study to evaluate the use of sarizotan in the treatment of respiratory abnormalities associated with Rett syndrome in children from 2 to less than 18 years of age with Rett syndrome and respiratory abnormalities **Study 10** Analysis of existing in house data on mechanism of action of sarizotan on Rett syndrome to provide efficacy assumptions in the paediatric population based on extrapolation

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 October 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes