EMA/208387/2017

European Medicines Agency decision

P/0089/2017

of 6 April 2017

on the acceptance of a modification of an agreed paediatric investigation plan for melatonin (Circadin), (EMEA-000440-PIP02-11-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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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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 European Medicines Agency's decision P/0117/2012 issued on 2 July 2012, the decision P/0257/2013 issued on 29 October 2013, the decision P/0012/2015 issued on 30 January 2015, the decision P/0244/2015 issued on 30 October 2015 and the decision P/0148/2016 issued on 14 June 2016,

Having regard to the application submitted by RAD Neurim Pharmaceuticals EEC Ltd on 8 February 2017 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 March 2017, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for melatonin (Circadin), prolonged-release tablet, ge-appropriate oral solid dosage form, 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 RAD Neurim Pharmaceuticals EEC Ltd, One Forbury Square, The Forbury, RG1 3EB - Reading, United Kingdom.

EMA/PDCO/123399/2017 Corr
London, 24 March 2017

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

EMEA-000440-PIP02-11-M05

Scope of the application

Active substance(s):

Melatonin

Invented name:

Circadin

Condition(s):

Treatment of insomnia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Prolonged-release tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

RAD Neurim Pharmaceuticals EEC Ltd

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, RAD Neurim Pharmaceuticals EEC Ltd submitted to the European Medicines Agency on 8 February 2017 an application for modification of the agreed paediatric investigation plan with a waiver as set out in the European Medicines Agency's decision P/0117/2012 issued on 2 July 2012, the decision P/0257/2013 issued on 29 October 2013, the decision P/0012/2015 issued on 30 January 2015, the decision P/0244/2015 issued on 30 October 2015 and the decision P/0148/2016 issued on 14 June 2016.

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

The procedure started on 21 March 2017.

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 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

1.1. Condition

Treatment of insomnia

The waiver applies to:

- all subsets of the paediatric population from birth to less than 2 years of age;
- for prolonged-release tablet and age-appropriate oral solid dosage form, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of insomnia

2.1.1. Indication(s) targeted by the PIP

Treatment of insomnia characterized by maintenance problems and sleep onset difficulties in children with pervasive developmental disorders and neurogenetic diseases

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)

Prolonged-release tablet, age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral solid dosage form.
Non-clinical studies	2	**Study 2** Repeated dose (14 day) toxicity study by oral gavage with melatonin in juvenile rats. (Study N) **Study 3** Repeated dose toxicity and toxicokinetic study in juvenile rats with melatonin from weaning to sexual maturity. (Study G)

Clinical studies	2	**Study 4** Open-label, pharmacokinetic cross over study of 2 mg and 10 mg prolonged release melatonin age-appropriate oral solid dosage form in children with neurodevelopmental disorders with sleep disturbances from 2 years to less than 18 years. (Study NEU child-PK) **Study 5** Randomized, double-blind, placebo controlled, study to investigate the efficacy and safety of melatonin to alleviate sleep disturbances in children with neurodevelopmental disabilities. (Study NEU-child) **Study 6** Deleted as result of EMEA-000440-PIP02-11-M02.

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 March 2017
Deferral for one or more studies contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s)

1. Treatment of insomnia

Authorised indications:

- Circadin is indicated as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over.

Authorised pharmaceutical form(s)

Prolonged-release tablet

Authorised route(s) of administration

Oral use