



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/602055/2013

European Medicines Agency decision

P/0257/2013

of 29 October 2013

on the acceptance of a modification of an agreed paediatric investigation plan for melatonin (Circadin) (EMA-000440-PIP02-11-M01) 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 European Medicines Agency's decision P/0117/2012 issued on 2 July 2012,

Having regard to the application submitted by RAD Neurim Pharmaceuticals EEC Ltd on 21 June 2013 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 13 September 2013, 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, age-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, Berkshire, United Kingdom.

Done at London, 29 October 2013

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/392758/2013

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

EMA-000440-PIP02-11-M01

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 21 June 2013 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/0117/2012 issued on 2 July 2012.

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

The procedure started on 17 July 2013.

Scope of the modification

Some timelines 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 Icelandic and the Norwegian Paediatric Committee members agree 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.

London, 13 September 2013

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

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	1	Measure 1: Development of an age-appropriate oral solid dosage form.
Non-clinical	2	Measure 2: Repeated dose (14 day) toxicity study by oral gavage with melatonin in juvenile rats. Measure 3: Repeated dose toxicity and toxicokinetic study in juvenile rats with melatonin from weaning to sexual maturity.

Area	Number of measures	Description
Clinical	2	Measure 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. Measure 5: Randomized, double-blind, placebo controlled, study to investigate the efficacy and safety of melatonin to alleviate sleep disturbances in children with neurodevelopmental disabilities. Measure 6: Open-label long-term (80 week) follow up safety and tolerability study on patients completing study 5.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By May 2016
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

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