EMA/405270/2012

European Medicines Agency decision

P/0117/2012

of 2 July 2012

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for melatonin (Circadin), (EMEA-000440-PIP02-11) 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 RAD Neurim Pharmaceuticals EEC Ltd on 11 April 2011 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 16 May 2012, in accordance with Article 18 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 melatonin (Circadin), prolonged-release tablet, age-appropriate oral solid 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 melatonin (Circadin), prolonged-release tablet, age-appropriate oral solid 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 melatonin (Circadin), prolonged-release tablet, age-appropriate oral solid 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 RAD Neurim Pharmaceuticals EEC Ltd, One Forbury Square, The Forbury, RG1 3EB - Reading, United Kingdom.

Done at London, 2 July 2012

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

EMA/405270/2012

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

EMEA-000440-PIP02-11

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

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Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, RAD Neurim Pharmaceuticals EEC Ltd submitted for agreement to the European Medicines Agency on 11 April 2011 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 18 May 2011.

Supplementary information was provided by the applicant on 27 February 2012. 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,
   - 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(es) and appendix.

London, 16 May 2012

On behalf of the Paediatric Committee
Dr Daniel Brasseur, 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. Studies

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

Area	Number of studies	Description
		than 18 years. 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 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.

EU Number	Invented name	Strength	Pharmaceutical Form	Route of administration	Packaging	Package size
EU/1/07/392/001	Circadin	2mg	Prolonged-release tablet	Oral use	Blister (PVC/PVDC/alu)	21
EU/1/07/392/002	Circadin	2mg	Prolonged-release tablet	Oral use	Blister (PVC/PVDC/alu)	20
EU/1/07/392/003	Circadin	2mg	Prolonged-release tablet	Oral use	Blister (PVC/PVDC/alu)	30