15 September 2022
EMA/847216/2022
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Melatonin Neurim

International non-proprietary name: melatonin

Procedure No. EMEA/H/C/005603/0000

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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1. Background information on the procedure

1.1. Submission of the dossier

The applicant RAD Neurim Pharmaceuticals EEC SARL submitted on 20 June 2022 an application for marketing authorisation to the European Medicines Agency (EMA) for Melatonin Neurim, through the centralised procedure. This application was submitted, in accordance with Article 82.1 of Regulation (EC) No 726/2004, as a multiple of Circadin authorised on 29 June 2007. The eligibility was granted by the CHMP on 26 March 2020.

The applicant applied for the following indication

Melatonin Neurim 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.

1.2. Legal basis, dossier content

The legal basis for this application refers to:

Article 10(c) of Directive 2001/83/EC – relating to informed consent from a marketing authorisation holder for an authorised medicinal product

The application submitted is

composed of administrative information with a letter from a MAH allowing the cross reference to relevant quality, non-clinical and clinical data.

This application is submitted as a multiple of Circadin authorised on 29 June 2007 in accordance with Article 82.1 of Regulation (EC) No 726/2004.

1.3. Information on Paediatric requirements

Not applicable

1.4. Information relating to orphan market exclusivity

1.4.1. Similarity

Pursuant to Article 8 of Regulation (EC) No. 141/2000 and Article 3 of Commission Regulation (EC) No 847/2000, the applicant did not submit a critical report addressing the possible similarity with authorised orphan medicinal products because there is no authorised orphan medicinal product for a condition related to the proposed indication.

1.5. Scientific advice

The applicant did not receive scientific advice on the development relevant for the indication subject to the present application:

1.6. Steps taken for the assessment of the product

The Rapporteur appointed by the CHMP was:

Rapporteur: Bruno Sepodes Co-Rapporteur: Anastasia Mountaki

CHMP Peer reviewer(s): N/A

The application was received by the EMA on	20 June 2022
The procedure started on	18 July 2022
The CHMP Rapporteur's first Assessment Report was circulated to all CHMP and PRAC members on	19 August 2022
The CHMP Co-Rapporteur's first Assessment Report was circulated to all CHMP and PRAC members on	N/A
The PRAC Rapporteur's first Assessment Report was circulated to all PRAC and CHMP members on	19 August 2022
The PRAC agreed on the PRAC Assessment Overview and Advice to CHMP during the meeting on	01 September 2022
The CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a marketing authorisation to Melatonin Neurim on	15 September 2022

2. Scientific discussion

This application has been submitted as an informed consent application in accordance with Article 10c of Directive 2001/83/EC as amended.

Accordingly, the MAH of the reference product, Circadin has provided consent to allow access to Module 2 to Module 5 of the initial dossier and any subsequent post-marketing procedures submitted, assessed and approved. The complete assessment history of Circadin is available on the EMA website.

The proposed indication for Melatonin Neurim is the same as the approved indication for the reference product.

2.1. Quality aspects

Since this application is an informed consent of the Circadin application, the quality data in support of the Melatonin Neurim application are identical to the up-to-date quality data of the Circadin dossier, which have been assessed and approved (including all post-marketing procedures).

2.2. Non-clinical aspects

Since this application is an informed consent of the Circadin application, the non-clinical data in support of the Melatonin Neurim application are identical to the up-to-date quality data of the Circadin dossier, which have been assessed and approved (including all post-marketing procedures).

The Environmental Risk Assessment (ERA) of Melatonin Neurim 2 mg prolonged-release tablets was performed according to the *Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use* EMEA/CHMP/SWP/4447/00 corr 2, 2006, and the Question and Answers document of the same Guideline (EMA/CHMP/SWP/44609/2010 Rev.1, 2016).

Melatonin Neurim is considered to be a true duplicate of Circadin since it will have the same of qualitative and quantitative composition in terms of active substance and the same pharmaceutical form. In this context, the authorization of the present applicant will not alter the concentration or distribution of the active substance in the environment. Therefore, Melatonin Neurim 2 mg prolonged-release tablets is not expected to pose a risk to the environment.

2.3. Clinical aspects

Since this application is an informed consent of the Circadin application, the clinical data in support of the Melatonin Neurim application are identical to the up-to-date quality data of the Circadin dossier, which have been assessed and approved (including all post-marketing procedures).

2.4. Risk Management Plan

The RMP is in line with the approved EU-RMP version 8.0 of the cross-referred medicinal product.

The CHMP considers that the risk management plan version 8 is acceptable.

2.5. Pharmacovigilance

2.5.1. Pharmacovigilance system

The CHMP considered that the pharmacovigilance system summary submitted by the applicant fulfils the requirements of Article 8(3) of Directive 2001/83/EC.

2.5.2. Periodic Safety Update Reports submission requirements

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web portal.

2.6. Product information

2.6.1. User consultation

A justification for not performing a full user consultation with target patient groups on the package leaflet has been submitted by the applicant and has been found acceptable for the following reasons: the package leaflet is identical in layout and core content to the approved leaflet for Circadin 2 mg prolonged-release tablets, additional readability testing is not considered necessary.

3. Benefit-Risk Balance

The overall benefit/risk balance of Melatonin Neurim is positive, subject to the conditions stated in section 'Recommendations'.

4. Recommendations

Based on the CHMP review of data on quality, safety and efficacy, the CHMP considers by consensus that the benefit-risk balance of Melatonin Neurim is favourable in the following indication:

Melatonin Neurim 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.

The CHMP therefore recommends the granting of the marketing authorisation subject to the following conditions:

Conditions or restrictions regarding supply and use

Medicinal product subject to medical prescription.

Other conditions and requirements of the marketing authorisation

- **Periodic Safety Update Reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web portal.

Conditions or restrictions with regard to the safe and effective use of the medicinal product

- **Risk Management Plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.