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**Datasheet for the decision
of 2 June 2016**

Case Number: T 0199/14 - 3.3.07

Application Number: 02760523.7

Publication Number: 1441702

IPC: A61K9/20

Language of the proceedings: EN

Title of invention:

METHOD FOR TREATING PRIMARY INSOMNIA

Applicant:

NEURIM PHARMACEUTICALS (1991) LIMITED

Relevant legal provisions:

EPC Art. 83, 84, 111(1)

Keyword:

Sufficiency of disclosure - (yes)

Claims - clarity - main request (no)

Appeal decision - remittal to the department of first instance
(yes)



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Case Number: T 0199/14 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 2 June 2016

Appellant: NEURIM PHARMACEUTICALS (1991) LIMITED
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted on 30 October 2013 refusing European patent application No. 02760523.7 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman D. Semino
Members: R. Hauss
P. Schmitz

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division, announced on 8 October 2013 and posted on 30 October 2013, refusing European patent application No. 02 760 523.7.

II. The documents cited in the examination and appeal proceedings included the following:

D25: Experimental report for EP 02 760 523.7, filed with letter of 24 January 2014

III. The decision under appeal was based on a sole request consisting of a set of six claims filed during oral proceedings before the examining division.

The independent claims of that request read as follows:

"1. Use of a prolonged release formulation comprising melatonin in unit dosage form, each unit dosage comprising 0.025 to 10 mg of melatonin, in the manufacture of a medicament for treating and improving the restorative quality of sleep in a patient suffering from primary insomnia characterized by non-restorative sleep, wherein the medicament comprises also at least one pharmaceutically acceptable diluent, preservative, antioxidant, solubilizer, emulsifiers, adjuvant or carrier.

4. A medicament for use in treating and improving the restorative quality of sleep in a patient suffering from primary insomnia characterized by non-restorative sleep which comprises a prolonged release formulation comprising melatonin in unit dosage form, each unit dosage comprising 0.025 to 10 mg of melatonin, and at least one pharmaceutically acceptable diluent,

preservative, antioxidant, solubilizer, emulsifiers, adjuvant or carrier."

In the decision under appeal, the examining division found that the subject-matter of claims 1 to 6 was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 83 EPC), since it had not been rendered credible that the desired effect of improving the restorative quality of sleep was achieved in respect of the population of patients younger than 55 years of age.

In example 3 of the application, it had been shown that in that age group, the administration of melatonin led to a significant worsening of the quality of sleep and daytime alertness compared to placebo. The explanation given in said example 3 for the negative results observed in younger patients was that, while older patients were more likely to suffer from sleep maintenance problems and non-restorative sleep, the younger population typically had sleep onset problems and their main problem might be sleep deficit and not non-restorative sleep. Thus melatonin was effective in primary insomnia related to non-restorative sleep, but could be detrimental to insomnia related to other aetiologies. Without corroborative evidence, that explanation was, however, regarded as speculative.

- IV. The applicant (appellant) lodged an appeal against that decision. With the statement setting out the grounds of appeal, the appellant submitted document D25, as well as a typewritten main request which corresponded to the request examined in the decision under appeal.
- V. In a communication issued in preparation for oral proceedings and advising the appellant of the board's preliminary opinion, the board raised *inter alia* an

objection under Article 84 EPC against the wording "treating ... the restorative quality of sleep" (see section 1 of the board's communication).

- VI. With letter dated 18 April 2016, the appellant submitted a new main request and two auxiliary requests.

Independent claims 1 and 4 of the **main request** are identical to the corresponding claims examined in the decision under appeal.

The **first auxiliary request** is identical to the main request, except for the deletion of the words "treating and" in claims 1 and 4.

- VII. Oral proceedings before the board took place on 2 June 2016.

- VIII. The appellant's arguments may be summarised as follows:

Article 84 EPC

In claims 1 and 4 of the main request, the term "treating" referred logically to the treatment of the specific indication (primary insomnia characterised by non-restorative sleep), whereas the term "improving" referred to the technical effect of such treatment (improving the quality of non-restorative sleep). Hence the wording of claims 1 and 4 was clear. The terms "treating" and "improving" did not relate to different categories or technical effects.

Article 83 EPC

The examining division had not applied the correct criteria in its assessment of sufficiency of disclosure. Since there existed no scientific reason for assuming that the efficacy of melatonin would be diminished in younger patients, and the application

provided a credible explanation for the worsening of the results which had been observed according to example 3 in that patient group, there could be no serious doubt that non-restorative sleep disorder could also be treated in younger patients. The examining division had failed to provide verifiable facts, in the form of citations of other documents, to substantiate any doubt raised.

As explained in document D25, further analysis of the data obtained in the clinical study of example 3 showed the efficacy of melatonin 2 mg prolonged-release treatment in a specially selected subgroup of younger patients which was believed to comprise a higher proportion of patients suffering from non-restorative sleep disorder.

- IX. The appellant requested that the decision under appeal be set aside and that the case be remitted to the department of first instance for further prosecution on the basis of the main request or the first or second auxiliary requests filed with letter of 18 April 2016.

Reasons for the Decision

1. Main request - Article 84 EPC
- 1.1 Claims 1 and 4 of the main request mention the indication "for (use in) treating and improving the restorative quality of sleep". While it is possible to treat a disorder or a patient suffering from a disorder, it is not quite clear what could be meant by treating a quality. The term "treating" in the context of claims 1 and 4 is either redundant because it should convey the same meaning as "improving", or unclear

because it is intended to have a different meaning which is not readily apparent.

1.2 According to the appellant, the skilled person would realise that the intended meaning was "treating a patient suffering from primary insomnia characterised by non-restorative sleep, thereby improving the quality of non-restorative sleep".

1.3 While this may well have been the actual intention of the drafter, the wording of a claim should be clear by itself and not require unnecessary analysis or speculation. As shown in point 1.2 above, if that was the intention, it would have been quite possible in the present instance to use unambiguous language.

1.4 Hence the board considers that the wording of claims 1 and 4 of the main request does not meet the requirements of Article 84 EPC, due to the usage of the term "treating" in the feature "treating ... the restorative quality of sleep".

2. First auxiliary request - Article 84 EPC

2.1 Due to the deletion of the words "treating and" in claims 1 and 4 of the first auxiliary request, the objection discussed in section 1 above does not apply to the claims of the first auxiliary request.

2.2 The board thus considers that claims 1 and 4 of the first auxiliary request meet the requirements of Article 84 EPC.

3. First auxiliary request - Article 83 EPC

3.1 The present claims do not define any age restriction with regard to the envisaged treatment of patients

suffering from primary insomnia characterised by non-restorative sleep.

- 3.2 Example 3 (page 12 to first paragraph of page 13) is the only part of the application providing data for patients under 55 years of age. It reports data obtained in a randomised, double-blind parallel group study with 131 primary insomnia patients aged 20 to 80 years. The subjects were treated for one week with placebo to establish baseline characteristics and then for three weeks with melatonin (2 mg per night of prolonged-release formulation) or placebo.

As implied in example 3 and confirmed by the appellant in D25 (page 2, bottom paragraph), all the subjects taking part in the study suffered from primary insomnia, but had not necessarily been recruited on the basis of non-restorative sleep, other possible types of primary insomnia being characterised by difficulty falling asleep or difficulty maintaining sleep rather than non-restorative sleep.

- 3.3 According to the assessment method used (which is described in example 2 on page 10 of the application), patients were asked on the last three days of the baseline and treatment periods to assess the quality of their sleep the previous night, the relevant question being: "How would you compare the quality of sleep using the medication with non-medicated (your usual) sleep?" The patients marked the level of their perceived quality of sleep on a 100 mm, non-hatched horizontal line with two endpoints. The left endpoint was labeled "more restless than usual" and the right endpoint was labeled "more restful than usual". The distance of the patient mark from the right endpoint in mm was measured, a reduction in value therefore

indicating a better sleep. The mean distance across the three nights was calculated.

- 3.4 Table 2 in example 3 of the application shows that in the "aged 55 years and over" patient group an improvement in sleep quality was observed (change in perceived quality of sleep, melatonin: -13.1, placebo: -7.4).
- 3.5 However, according to page 12, paragraph 2 of the application: "Surprisingly, it was found that in patients <55 years of age there was a significant worsening of the quality of sleep compared to placebo" (change in perceived quality of sleep, melatonin: -1.6, placebo: -13.7).
- 3.6 This is attributed, in the paragraph bridging pages 12 and 13 of the application, to younger people typically not suffering from non-restorative sleep disorder but having other sleep problems, in particular sleep deficit due to sleep onset problems, while the elderly are more likely to have maintenance and non-restorative sleep problems. In that context, the application refers to two scientific publications reporting age-dependent prevalence. The results shown in table 2 of example 3 are taken to indicate that melatonin may be detrimental to insomnia related to other aetiologies, e.g. sleep deficit (page 13, lines 2 to 5).
- 3.7 While that may be an explanation for the difference observed in the younger patient group, the only conclusion which might be drawn on that basis is that the data as presented in example 3 may be unsuitable to show the effect of the medicament on younger patients suffering specifically from non-restorative sleep disorder.

3.8 The observed results themselves raise serious doubts as to whether a beneficial effect may be obtained.

No corroborative evidence with regard to the actual prevalence of non-restorative sleep in patients who took part in the study of example 3 and no further evidence of the effect of melatonin on younger patients known to suffer from non-restorative sleep is provided in the application.

3.9 On that basis, the examining division was thus correct in having serious doubts that the alleged technical effect could be obtained over the entire scope claimed, which includes the treatment of patients under 55 years of age, said serious doubts being substantiated by the diverging experimental results which were reported in the application itself with regard to younger patients.

3.10 Since a possible explanation for the divergence is given in the application, namely that younger patients are less likely to suffer from non-restorative sleep, it is, however, appropriate to take the appellant's supplementary evidence, provided subsequently in D25, into account, which may serve to verify whether the explanation is well-founded.

3.11 According to D25, an analysis of covariance was performed on the change in perceived quality of sleep after three weeks of melatonin treatment, using the data obtained in the study of example 3. The covariate "quality of sleep at baseline" was found to be statistically significant, indicating that the extent of response to the medicament has a correlation with the perceived quality of sleep at baseline.

3.12 As reported in D25, the patients of the study described in example 3 of the application were subdivided into

groups, based on whether at baseline they had quality of sleep below or above the median value of perceived quality of sleep for these patients, and the change in quality of sleep after 3 weeks' treatment with melatonin 2 mg was calculated for the subgroups separately. The median value was 51 mm (thus close to 50 mm, signifying unchanged perceived sleep quality).

3.13 The majority of the patients whose sleep quality at baseline was worse than the median value were aged 55 years and over. The quality of sleep improved with melatonin 2 mg in the younger as well as in the older patients in this group. As far as patients were concerned whose quality of sleep at baseline was better than the median value, quality of sleep did not improve with administration of melatonin in either age group (see D25: table 3).

3.14 The appellant supported the view that the group of patients having quality of sleep at baseline worse than the median value of the perceived quality of sleep contains a higher percentage of patients suffering from non-restorative sleep than the undistinguished group of patients suffering from primary insomnia. This, in the view of the appellant, is due to the fact that patients suffering from non-restorative sleep disorder would tend to perceive their quality of sleep as bad and therefore more often than not even as worse than usual.

While the board considers that the selection of patients suffering from non-restorative sleep disorder could have been done in a more direct manner, the analysis of the appellant concerning the higher occurrence of patients suffering from that disorder in the identified group is found plausible.

As the covariance analysis shows that in those patients the quality of sleep improved with administration of melatonin in both age groups while for those having a quality of sleep at baseline better than the median value the quality of sleep diminished, the analysis shows that the explanation given in example 3 is credible and supported by data.

In view of this, the serious doubts present on the basis of the results in the application alone have been overcome.

- 3.15 As a consequence, the board concludes that the requirements of Article 83 EPC are met.

- 4. Remittal (Article 111 (1) EPC)
 - 4.1 The decision under appeal is concerned exclusively with objections under Article 83 EPC regarding sufficiency of disclosure.

 - 4.2 In accordance with the appellant's request, the board finds it appropriate to remit the case to the department of first instance, since the first instance has not yet decided on novelty and inventive step.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance for further prosecution on the basis of the first auxiliary request.

The Registrar:

The Chairman:



S. Fabiani

D. Semino

Decision electronically authenticated