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Datasheet for the decision of 3 November 2021

Case Number: T 2056/17 - 3.3.01

Application Number: 13004798.8

Publication Number: 2695618

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Language of the proceedings: EN

Title of invention:

Pharmaceutical composition comprising lacosamide and levetiracetam for use in the treatment of epilepsy

Patent Proprietor:

UCB Pharma GmbH

Opponents:

Helm AG
ZAKLADY FARMACEUTYCZNE POLPHARMA S.A.

Headword:

Combination lacosamide-levetiracetam/UCB

Relevant legal provisions:
EPC Art. 54, 76(1)

Keyword:
Main request and auxiliary request 1 - novelty of second medical use (no)
Auxiliary request 2 - subject-matter extends beyond content of earlier application (yes)
Auxiliary request 3 - no examination (reformatio in peius)

Decisions cited:
G 0009/92

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Case Number: T 2056/17 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 3 November 2021

Appellant: (Patent Proprietor)	UCB Pharma GmbH Alfred-Nobel-Strasse 10 40789 Monheim (DE)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Respondent: (Opponent 1)	Helm AG Nordkanalstrasse 28 20097 Hamburg (DE)
Representative:	Uexküll & Stolberg Partnerschaft von Patent- und Rechtsanwälten mbB Beselerstraße 4 22607 Hamburg (DE)
Respondent: (Opponent 2)	ZAKLADY FARMACEUTYCZNE POLPHARMA S.A. ul. Pelplinska 19 83-200 Starogard Gdanski (PL)
Representative:	Chmurzynski, Sedzimir Lech Polpharma S.A. ul. Pelplinska 19 PL-83-200 Starogard Gdanski (PL)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 4 July 2017 concerning maintenance of the European Patent No. 2695618 in amended form.**

Composition of the Board:

Chairman	A. Lindner
Members:	J. Molina de Alba
	L. Bühler

Summary of Facts and Submissions

I. This appeal by the patent proprietor (appellant) is directed against the opposition division's interlocutory decision rejecting the patent proprietor's main request (patent as granted) and auxiliary requests 1 to 3 and finding that European patent No. 2 695 618 as amended in the form of auxiliary request 4 and the invention to which it relates met the requirements of the EPC.

II. European patent No. 2 695 618 stems from European patent application 13004798.8 which was filed as a divisional of European patent application 07764676.8, published as WO 2007/144195 (earlier application).

III. The patent had been granted with eight claims. Claim 1 as granted reads as follows.

"*1. A pharmaceutical combination for use in the prevention, alleviation or/and treatment of epileptic seizures, which comprises a separate dosage form comprising (a) a first composition comprising lacosamide and (b) a second composition comprising levetiracetam, wherein the compositions (a) and (b) are provided in distinct preparations (separate dosage forms), which are administered simultaneously and/or subsequently, wherein said separate dosage forms are co-presented in separate packaging, or are separately packaged and available for sale independently of one another, but are co-marketed or co-promoted for simultaneous and/or subsequent administration.*"

IV. The following document is referred to in the present decision.

D2: D. Jatuzis *et al.*, Epilepsia, Vol. 46, Suppl. 8, 2005, p. 170

V. Two oppositions were filed against the patent on the grounds that the claimed subject-matter lacked novelty and inventive step, contained subject-matter excluded from patentability, was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, and extended beyond the content of the earlier application as filed (Article 100(a), (b) and (c) EPC).

VI. In the decision under appeal, the opposition division considered, among other things, that:

- claim 1 of the patent as granted (main request) contained a combination of technical and non-technical features; as the latter were not limiting, the subject-matter of claim 1 was not novel over the disclosure of document D2
- for the same reasons, the subject-matter of claim 1 of either of auxiliary requests 1 and 3 also lacked novelty
- auxiliary request 2 contravened Rule 80 EPC
- auxiliary request 4 met the requirements of the EPC

VII. The patent proprietor filed an appeal requesting that the opposition division's decision be set aside and that the patent be maintained as granted. With its statement of grounds of appeal, the appellant filed three sets of claims as auxiliary requests 1 to 3. Auxiliary request 1 was identical to auxiliary request

1 on which the decision under appeal was based. Auxiliary request 2 was a new request. Auxiliary request 3 was identical to the request considered allowable by the opposition division.

Claim 1 of auxiliary request 1 differs from claim 1 as granted in that the option that compositions (a) and (b) are co-presented in separate packaging has been deleted.

Claim 1 of auxiliary request 2 differs from claim 1 as granted in that the pharmaceutical combination is specified as being "in form of a two component drug".

VIII. The board summoned the parties to oral proceedings, in line with the appellant's request.

In a subsequent communication, the board gave its preliminary opinion. Among other things, the board raised doubts as to the novelty of the subject-matter of claim 1 of the main request and auxiliary request 1 over D2. It also asked the appellant to indicate the basis for claim 1 of auxiliary request 2 in the earlier application as filed.

IX. The respondents (opponents 1 and 2), which had not made any submissions during the appeal proceedings, withdrew their oppositions with the letters dated 31 May 2021 and 16 July 2021, respectively. Thus, they ceased to be parties to these proceedings.

X. The appellant reacted to the board's preliminary opinion with a letter dated 1 October 2021.

XI. Oral proceedings were held before the board on 3 November 2021. At the end of the oral proceedings, the board announced its decision.

XII. The appellant's arguments, where relevant to the present decision, can be summarised as follows.

The patent invention was based on the finding that the combined effect of lacosamide and levetiracetam resulted in a synergistic reduction of epileptic seizures. As this combined effect could only be achieved if the two drugs were simultaneously present in the patient's plasma to exert their respective anti-convulsive activity in conjunction, it was essential that lacosamide and levetiracetam be administered simultaneously and/or subsequently. This administration was ensured by the feature in claim 1 as granted that lacosamide and levetiracetam are separately packaged and available for sale independently of one another but are co-marketed or co-promoted for simultaneous and/or subsequent administration. Thus, in line with decision G 2/08, claim 1 defined a second medical use characterised by a dosage regime which was essential to the invention and had a limiting effect on the claimed subject-matter. The feature that lacosamide and levetiracetam were separately packaged but co-marketed or co-promoted for simultaneous and/or subsequent administration was an essential element of the dosage regime and had to be taken into account for the examination of novelty and inventive step.

The clinical trials reported in D2 did not anticipate the subject-matter of claim 1 as granted because they did not disclose any of the following features:

- simultaneous and/or subsequent administration of lacosamide and levetiracetam
- co-marketing or co-promotion for simultaneous and/or subsequent administration
- combination therapy

Regarding the simultaneous and/or subsequent administration, D2 indicated that lacosamide was given twice daily but failed to specify when and how often antiepileptic drugs, in particular levetiracetam, were taken. The drugs could have been administered in a regime which was neither simultaneous nor subsequent. For instance, they could have been provided intermittently to produce an alternate rather than a combined effect.

With respect to co-marketing or co-promotion of the drugs, the trial in D2 was double-blinded so that neither the investigators nor the patients knew what they were administering or receiving.

Lastly, the trial in D2 did not look at combination therapy but lacosamide as adjunctive therapy. It was common general knowledge that adjunctive therapy was required for the marketing authorisation of drugs which, for ethical reasons, could not be tested alone for direct comparison with untreated patients. Although adjunctive therapy required a baseline treatment, its focus was on the effect produced beyond the baseline. Thus, the trials in D2 aimed at showing the effect of lacosamide alone, and the baseline treatment with concomitant antiepileptic drugs was irrelevant. The standard required by regulatory authorities for a combination therapy was more demanding. It required additional tests and a different set-up. The clinical

set-up of D2, designed for adjunctive therapy, did not allow drawing any conclusion on a combination therapy.

Claim 1 of auxiliary request 2 did not contain subject-matter extending beyond the disclosure of the earlier application as filed. The combination of lacosamide and levetiracetam was one of the particularly preferred embodiments illustrated in the examples (page 51, lines 6-10; Figure 5 and tables 2 to 4), each of which could be formulated either as single or separate dosage forms, according to page 22 of the earlier application.

XIII. The appellant's final request was that the decision under appeal be set aside and that the patent be maintained as granted (main request) or, alternatively, that the patent be maintained in amended form on the basis of the claims of one of auxiliary requests 1 to 3, all filed with the statement of grounds of appeal.

Reasons for the Decision

1. The appeal is admissible. It meets the requirements of Articles 106 to 108 and Rule 99(2) EPC.

2. Main request - novelty (Article 54 EPC)

2.1 Document D2 discloses the result of clinical trials which evaluate the effect of oral lacosamide (LCM) on concomitant antiepileptic drugs (AEDs). One of the AEDs is LVT, which in the opposition proceedings was assumed to be levetiracetam (decision, page 14, paragraph 33). The appellant did not contest this assumption

(statement of grounds of appeal, page 7, line 4). The board sees no reason to differ.

The trials in D2 aimed at investigating the efficacy and safety of oral LCM as adjunctive therapy in subjects with uncontrolled, partial seizures taking one or two concomitant AEDs, including LVT. First, the plasmatic baseline of the AEDs was established during eight weeks. Then, patients were treated concomitantly with placebo, 200, 400 or 600 mg/day LCM twice daily (bid). During the first six weeks of concomitant treatment, LCM was titrated to the final dose. After that, the treatment was maintained for 12 weeks. The dose of AEDs was maintained constant during the whole trial.

The authors of D2 concluded from the trials that the concomitant administration of LCM did not affect the mean plasma concentration of AEDs and that it reduced patients' seizure frequency.

2.2 The design of the trial in D2, where AEDs constituted a baseline treatment and LCM was later added in concomitance, implies that LVT and LCM were administered in separate dosage forms. This was not contested by the appellant (statement of grounds, point 2.5.1).

2.3 Given that AEDs constituted the baseline treatment, their plasma levels had to be sufficient to provide a therapeutic effect across the whole trial. Moreover, as LCM was administered concomitantly during 12 weeks to prevent the partial seizures that AEDs could not control, AEDs and LCM had to be present in plasma simultaneously at therapeutic levels. Thus, contrary to the appellant's contention, AEDs and LCM necessarily

acted in combination. Moreover, the only possible option for achieving such a combined effect was that AEDs and LCM were administered simultaneously and/or subsequently.

2.4 The appellant's arguments that D2 does not disclose a combination therapy or that AEDs and LCM in D2 were not administered simultaneously and/or subsequently are not convincing.

At the oral proceedings before the board, the appellant put forward that, rather than a combination therapy, D2 disclosed the use of LCM as adjunctive therapy. Thus, although AEDs had to be added as a baseline treatment for ethical reasons, the focus of D2 was exclusively on the individual effect of LCM. Adjunctive and combination therapy had different meanings in the context of marketing authorisations: they implied different clinical set-ups and required different experimental evidence. Therefore, D2 did not allow the reader to draw any conclusion on a combination therapy.

The board disagrees. There is no basis in claim 1 for interpreting the feature "pharmaceutical combination" narrowly or restricted to the meaning used in the specific context of marketing authorisations. As put forward above, the design of the clinical trials in D2 imply the combined effect of LCM and LVT. Thus, the separate compositions of LCM and LVT administered in D2 constituted a pharmaceutical combination within the meaning of claim 1.

This also means that the appellant's allegation (statement of grounds of appeal, point 2.4 and letter of 1 October 2021, page 6, paragraphs 2-4) that LCM and LVT could have been administered in a alternating or

intermittent manner which would be different from simultaneous and/or subsequent administration, cannot succeed. It is notorious that the combined action of two actives can only be achieved if they are administered simultaneously and/or subsequently.

2.5 Hence, in accordance with claim 1, D2 discloses a pharmaceutical combination for use in the treatment of epileptic seizures which comprises a separate dosage form comprising (a) a first composition comprising LCM and (b) a second composition comprising LVT, where the compositions (a) and (b) are provided in distinct preparations, i.e. packaged separately, and administered simultaneously and/or subsequently.

2.6 Regarding the feature in claim 1 that the actives are available for sale independently of one another but are co-marketed or co-promoted for simultaneous and/or subsequent administration, the board notes the following.

The effective treatment of epileptic seizures according to both claim 1 and D2 is achieved by the simultaneous and/or subsequent administration of the separate dosage forms of LCM and LVT. The fact that these dosage forms are available for sale independently of one another but co-marketed or co-promoted for simultaneous or subsequent administration does not render the therapeutic treatment in claim 1 different from that in D2. In both cases, the therapeutic effect is the same, it is achieved on patients having the same physiologic and pathologic state, using the same combination of active ingredients, administered by the same route and with the same dosage regime. In other words, claim 1 and D2 relate to an identical clinical situation which is treated with the same therapeutic measures.

Therefore, claim 1 does not define a new specific use within the meaning of Article 54(5) EPC.

The board rejects the appellant's argument that co-marketing and co-promotion of the separate dosage forms for simultaneous and/or subsequent administration belongs to the dosage regime and that it ensures the success of the therapeutic treatment. The effectiveness of the therapy lies in the fact that LCM and LVT are administered simultaneously and/or subsequently. This is the essential feature of the dosage regime, and it is present in D2. As put forward above, how the actives are co-promoted or co-marketed neither changes the clinical situation nor contributes to the therapeutic effect.

2.7 The board therefore concludes that the subject-matter of claim 1 lacks novelty, contrary to Article 54 EPC.

3. Auxiliary request 1 - novelty (Article 54 EPC)

Claim 1 of auxiliary request 1 derives from claim 1 of the main request by removing the feature that the separate dosage forms are co-presented in separate packaging. Thus, claim 1 is limited to the alternative that the separate dosage forms are separately packaged and available for sale independently of one another but are co-marketed or co-promoted for simultaneous and/or subsequent administration. This option is the one discussed above in relation to claim 1 of the main request and found to lack novelty over D2.

Therefore, claim 1 of auxiliary request 1 does not meet the requirements of Article 54 EPC either.

4. Auxiliary request 2 - amendments (Article 76(1) EPC)

Claim 1 of auxiliary request 2 contains, among other features, a pharmaceutical combination which comprises as separate dosage forms a composition (a) comprising LCM and a composition (b) comprising LVT. At the oral proceedings before the board, the appellant submitted that the basis for these features in the earlier application as filed was the particularly preferred embodiments illustrated in the examples (page 51, lines 6-10; Figure 5 and tables 2 to 4), each of which could be formulated either as single or separate dosage forms, according to page 22.

The board notes that the earlier application discloses on page 13, lines 32-33 the combination of LCM and LVT as a particularly preferred embodiment. This embodiment is illustrated in the examples on page 51, lines 6-10, and page 55, line 29 and in Figure 5 and tables 2-4. However, the combination of LCM and LVT is merely one among a list of other particularly preferred embodiments disclosed on pages 13-15 and illustrated in the examples on page 51, lines 1-6 and in Figures 1-7 and tables 1-4. Those other particularly preferred embodiments include, for instance, the combination of LCM with lamotrigine, valproate, carbamazepine, phenytoin, topiramate and gabapentin.

On page 22, lines 3-7, the earlier application discloses that the compound of Formulae (I), (II) and/or (III) (e.g. LCM, see page 21, lines 32-33) and the compound (b) may be formulated in one pharmaceutical preparation (single dosage form) or in two or more distinct preparations (separate dosage forms). These two possibilities are reiterated in the subsequent passages on page 22, lines 11-20.

Thus, according to the earlier application, the combination of LCM with LVT is one among several equivalent options, and the formulation of the pharmaceutical combinations in separate dosage forms is also one out of two equally preferred choices. The appellant has failed to demonstrate that the earlier application discloses a link between the LCM/ LVT combination and the formulation in separate dosage forms. Therefore, the board holds that the earlier application does not directly and unambiguously disclose a pharmaceutical combination comprising LCM and LVT formulated in separate dosage forms.

Consequently, claim 1 of auxiliary request 2 contains subject-matter which extends beyond the content of the earlier application as filed, contrary to Article 76(1) EPC.

5. *Auxiliary request 3 - prohibition of reformatio in peius*

This request is identical to the one considered allowable by the opposition division. Given that the patent proprietor is the only appellant in these proceedings, the prohibition of *reformatio in peius* does not allow the board to examine auxiliary request 3 (see G 9/92, Headnote I). This request is equivalent to a dismissal of the appeal and a maintenance of the patent in amended form as decided by the opposition division.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated