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Datasheet for the decision of 19 January 2016

Case Number: T 2399/12 - 3.3.07

Application Number: 08725456.1

Publication Number: 2120875

IPC: A61K9/12, A61K31/48, A61K9/72, A61P25/06

Language of the proceedings: EN

Title of invention:
METHOD OF THERAPEUTIC ADMINISTRATION OF DHE TO ENABLE RAPID RELIEF OF MIGRAINE WHILE MINIMIZING SIDE EFFECT PROFILE

Applicant:
Map Pharmaceuticals Inc.

Relevant legal provisions:
EPC Art. 83, 84, 111(1), 116(1)

Keyword:
Right to be heard - no oral proceedings before board of appeal
Sufficiency of disclosure - (yes)
Claims - clarity (yes)
Appeal decision -
remittal to the department of first instance (yes)

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Case Number: T 2399/12 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 19 January 2016

Appellant: (Applicant)	Map Pharmaceuticals Inc. 2525 Dupont Drive Irvine, California 92612 (US)
Representative:	Sexton, Jane Helen J A Kemp 14 South Square Gray's Inn London WC1R 5JJ (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 20 June 2012 refusing European patent application No. 08725456.1 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	J. Riolo
Members:	D. Semino
	P. Schmitz

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division announced at the oral proceedings on 22 May 2012 refusing European patent application No. 08 725 456.1.

II. The decision was based on a single set of claims filed with letter of 2 September 2011, whereby claim 1 read as follows:

"1. A compound which is dihydroergotamine or a complex, chelate, salt, hydrate, polymorph, or ion pair thereof for use in a method of treatment of migraine in a human individual;
wherein the treatment comprises delivery by pulmonary inhalation by a device comprising a dry powder inhaler, nebulizer, vaporizer, pressurized metered dose inhaler, or breath activated pressurized metered dose inhaler, of a total dose of dihydroergotamine, or a complex, chelate, salt, hydrate, polymorph or ion pair thereof of from 0.1 to 10 mg per migraine attack; and the dose being in a solid, liquid or aerosol formulation adapted for administration by said device
(i) to deliver the dihydroergotamine, or a complex, chelate, salt, hydrate, polymorph or ion pair thereof at such a rate that a mean peak plasma concentration (C_{max}) of dihydroergotamine is less than 15,000 pg/ml and a mean time to C_{max} (T_{max}) of dihydroergotamine is less than 30 minutes; or
(ii) to deliver the dihydroergotamine, or a complex, chelate, salt, hydrate, polymorph or ion pair thereof at a rate such that a mean peak plasma concentration (C_{max}) of 8-hydroxy dihydroergotamine is less than 1,000 pg/ml, and a mean time to C_{max} (T_{max}) of 8-hydroxy dihydroergotamine is less than 90 minutes."

The set of claims included two further independent claims (device claim 14 and use claim 17), which included alternative features (i) and (ii) of claim 1.

III. In the decision under appeal, document D1 (WO-A-2005/025506) was cited *inter alia*.

IV. The decision under appeal can be summarised as follows:

With regard to claim 1, while it was not contested that the required C_{max} and T_{max} constituted a solution to the problem of lowering the side effects while treating migraine with dihydroergotamine and the tests for measuring C_{max} and T_{max} were considered prima facie known to the skilled person, there was no indication in the application of how to obtain a suitable formulation which could be used to obtain the required C_{max} and T_{max}. In particular, the examples failed to disclose any suitable starting point for carrying out the invention, so that the skilled person was not in a position to repeat the invention without undue experimentation. Document D1 confirmed that finding the correct formulation was not straightforward. In view of that, no exception could be made to allow an invention defined by the result to be achieved and the requirements of Article 84 EPC were not met. For the same reasons, the invention was not sufficiently disclosed contrary to the requirements of Article 83 EPC. The same applied to independent claims 14 and 17.

V. The applicant (appellant) filed an appeal against that decision.

VI. With the statement setting out the grounds of appeal, the appellant requested that the decision under appeal

be set aside and a patent be granted on the basis of one of the three sets of claims filed as main request and as auxiliary requests 1 and 2 therewith. Oral proceedings were requested in case the Board were not minded to grant the main request.

The main request included independent claims 1 (product claim) and 14 (use claim), wherein claim 1 read as follows:

"1. A compound which is dihydroergotamine or a salt, hydrate, polymorph, or ion pair thereof for use in a method of treatment of migraine in a human individual; wherein the treatment comprises delivery by pulmonary inhalation by a device comprising a dry powder inhaler, nebulizer, vaporizer, pressurized metered dose inhaler, or breath activated pressurized metered dose inhaler, of a total dose of dihydroergotamine, or a salt, hydrate, polymorph or ion pair thereof of from 0.1 to 10 mg per migraine attack;
and the dose being in a solid, liquid or aerosol formulation adapted for administration by said device to administer the dihydroergotamine, or a salt, hydrate, polymorph or ion pair thereof at such a rate that the peak plasma concentration (C_{max}) of dihydroergotamine is less than 15,000 pg/ml and the time to C_{max} (T_{max}) of dihydroergotamine is less than 30 minutes after administration."

Use claim 14 included the same condition on C_{max} and T_{max} as claim 1.

Document E1 (Shrewsbury et al, Headache, volume 48, 2008, pages 355-367) was also annexed to the statement *inter alia*.

VII. In a communication sent in preparation of oral proceedings, the Board gave a positive opinion on sufficiency and clarity for the main request (point 1) and expressed its intention to remit the case to the department of first instance for further prosecution, since the further patentability requirements had not yet been examined (point 2).

VIII. By letter dated 12 October 2015, the appellant withdrew the request for oral proceedings on the understanding that the case be remitted to the department of first instance for further prosecution. The request for oral proceedings was maintained in case the Board intended to take any action other than remitting to the department of first instance or granting the application.

IX. Following that letter, the oral proceedings were cancelled.

X. The appellant's arguments on sufficiency and clarity can be summarised as follows:

According to the case law, an application may be objected to for lack of sufficiency, only if there are serious doubts, substantiated by verifiable facts. This was not the case for the present application in which parameters were used with which the skilled person, who knew plasma concentrations and how to measure them, was very familiar. Moreover, claim 1 itself by defining the drug, the medical condition to be treated, the route of administration, the device used to administer the drug and the dosage together with the pharmacokinetic profile, and the examples in the application, in which the desired result was achieved by choosing the route, the device and the dosage according to the claim, gave

sufficient information on how to carry out the invention. The detailed information contained throughout the description and the examples resulted therefore in a strong presumption in favour of sufficiency, which was not countered by any evidence supporting the contrary. For these reasons the claims met the requirements of Article 83 EPC. As the objections under Article 84 EPC in the decision were based on the same arguments, the reasons given with respect to sufficiency were equally valid to rebut the objections under Article 84 EPC.

Reasons for the Decision

Article 116(1) EPC

1. As the present decision grants the request of the appellant to set aside the decision and the request for oral proceedings is conditional to a decision being taken other than remittal or grant, the decision may be taken in writing while fulfilling the requirements of Article 116(1) EPC.

Sufficiency and clarity

2. In the decision under appeal the requirements of Articles 83 and 84 EPC were considered not to be met, as there was no indication in the application of how to obtain a suitable formulation which could be used to obtain the required C_{max} and T_{max}, as the examples failed to disclose any suitable starting point for carrying out the invention and as document D1 confirmed that finding the correct formulation was not straightforward. On the other side, it was not contested that the required C_{max} and T_{max} constituted a solution to the problem of lowering the side effects

while treating migraine with dihydroergotamine and the tests for measuring C_{max} and T_{max} were considered prima facie known to the skilled person.

2.1 The Board agrees with the findings that the given values constitute a solution to the posed problem and that the tests for measuring the parameters are known.

2.2 As to the lack of an indication of how to obtain a formulation with the required C_{max} and T_{max}, the Board notes that dihydroergotamine in a form suitable for pulmonary inhalation is known from document D1 (cited in the application in paragraph [0082]) and that the teaching can be drawn from the application (see in particular paragraphs [0077] to [0084]) including in particular example 1 (paragraphs [0100] to [0103] and figure 2) that by administering through pulmonary inhalation a dosage comparable to the one normally administered by intravenous delivery the C_{max} is reduced of an order of magnitude with respect to intravenous administration and the T_{max} does not change significantly, obtaining thereby values within the ranges of claim 1.

2.3 The fact that some detail is missing in example 1 (the exact formulation and the exact device) is in this respect not relevant, as long as the teaching is credible and there is is no counter-evidence available on file.

2.4 On top of that, further evidence is available on file to support the credibility of the teaching.

2.4.1 Document D1 shows the pharmacokinetic profile of dihydroergotamine administration to dog by pulmonary inhalation and by intravenous delivery (page 15, line

15 to 26, table 4, figure 1). Also in this case T_{max} is similar in the two cases and C_{max} is reduced of an order of magnitude in pulmonary inhalation with respect to intravenous administration even if the dosage is higher (1 mg vs 0.5 mg). Even though the value of C_{max} in figure 1 of D1 is beyond what is required in claim 1, it refers to a high dosage of 1 mg administered to a dog, so that it is credible to expect that administration to a human being in a proper dosage (or administration of a lower dosage to a dog) will result in a value of C_{max} in the required range.

2.4.2 Document E1 also shows that administration of dihydroergotamine by pulmonary inhalation as opposed to intravenous delivery results in rapid systemic absorption, short peak time (T_{max} of 12 minutes) and lower peak values (C_{max}) well within the ranges in claim 1 (abstract, study design on page 357 and result starting on page 359, in particular table 3 and figure 3). In this respect it is relevant to note that document E1 constitutes post-published evidence, which is not strictly necessary, but supports the teaching in the application without contradicting it or indicating the need to control other parameters not disclosed in the application.

2.5 With the evidence available on file, it is therefore credible that, by choosing the proper mode of administration (pulmonary inhalation) and an appropriate dosage (similar to the one administered intravenously), it is expected to obtain the claimed results. On that basis, the Board considers that there are no facts, nor any serious doubts which could support an objection of insufficiency of disclosure due to the presence of the conditions on C_{max} and T_{max}.

2.6 In view of that, the requirements of Article 83 EPC are met.

2.7 As a lack of clarity was found by the examining division on exactly the same grounds as an insufficiency of disclosure, the Board concludes that also the requirements of Article 84 EPC are fulfilled for the same reasons as outlined above.

2.8 As a final remark, the Board would like to point out that the conclusions reached are valid with the evidence available on file, which implies that, if further evidence were available at a later point, e.g. to show that the result may not be achieved following the teaching of the prior art in view of further conditions which should be met, the issue could be reopened.

Remittal

3. The examining division only decided that the requirements of Articles 83 and 84 EPC were not met and did not address the further requirements of the convention.

3.1 While pursuant to Article 111(1) EPC the Board of Appeal may either exercise any power within the competence of the department which was responsible for the decision or remit the case for further prosecution, in a case such as the one at hand, where fundamental requirements of the convention have not yet been examined and decided by the department of first instance, the case is normally remitted to the first instance, so that the outstanding issues may be properly examined by two instances.

3.2 Thus, in view of the above considerations, the Board considers it appropriate to remit the case to the examining division for further prosecution on the basis of the claims according to the main request.

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 main request filed with the statement setting out the grounds of appeal.

The Registrar: The Chairman:

S. Fabiani J. Riolo

Decision electronically authenticated