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Datasheet for the decision of 22 April 2015

Case Number: T 1023/11 - 3.3.07

Application Number: 07008503.0

Publication Number: 1849462

IPC: A61K9/54, A61K31/195, A61P21/02, A61P25/14

Language of the proceedings: EN

Title of invention:
A method of alleviating signs and symptoms of Spasticity

Applicant:
Sun Pharma Advanced Research Company Limited

Headword:

Relevant legal provisions:
EPC Art. 123(2), 54, 54(5), 56

Keyword:
Novelty - (yes)
Inventive step - (yes)

Decisions cited:

Catchword:

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Case Number: T 1023/11 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 22 April 2015

Appellant: (Applicant)	Sun Pharma Advanced Research Company Limited 17/B Mahal Industries Estate OFF, Mahakali Caves Road Andheri (East) Mumbai 400 093 (IN)
Representative:	Atkinson, Jonathan David Mark HGF Limited Belgrave Hall Belgrave Street Leeds LS2 8DD (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 16 December 2010 refusing European patent application No. 07008503.0 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	J. Riolo
Members:	A. Usuelli
	W. Ungler

Summary of Facts and Submissions

I. The appeal of the applicant (appellant) lies from the decision of the examining division announced at the oral proceedings on 17 November 2010 to refuse European patent application No. 07008503.0.

II. The documents cited during the examination proceedings included the following:

D1: US 2004/0180088
D2: WO2005/019163
D4: WO 2005/120435

III. The decision was based on a main request filed during the oral proceedings.

Claim 1 of the main request read as follows:

"1. An oral controlled drug delivery system comprising an effective daily dose of baclofen or its pharmaceutically acceptable salt for use, by orally administering once in a day to human patients suffering from signs and symptoms of spasticity, in the treatment of spasticity, wherein a reduced level of sedation is experienced by the patients relative to conventional baclofen therapy administered in the form of immediate release tablets in the same total daily dosage 3 times a day."

IV. The examining division's decision may be summarised as follows:

a) Document D1 disclosed a drug delivery system which could contain various active ingredients, including the muscle relaxant baclofen. It was

furthermore mentioned that the formulation was suitable for once daily administration. Although the use of the formulation in the treatment of the signs and symptoms of spasticity was not explicitly mentioned in D1, this use was to be regarded as implicitly disclosed, since it was generally known that the muscle relaxants had this therapeutic application. As to the reduction of the level of sedation, this effect did not lead to the use of baclofen for a hitherto unknown purpose. Accordingly, the subject-matter claimed did not comply with the requirements of Article 54 EPC.

b) Document D1 was regarded as the closest prior art for the assessment of inventive step. Starting from the assumption that the reduction of the sedation level represented a distinguishing feature, the technical problem was formulated as the provision of a better therapy for the treatment of signs and symptoms of spasticity which caused less sedation. D1 taught that controlled-release delivery systems lowered the incidence of side effects. Therefore, the subject-matter claimed was not inventive.

V. The appellant lodged an appeal against that decision. With the statement setting out the grounds of appeal filed with letter dated 20 April 2011, he submitted a set of claims as main request, this set of claims being identical to the one refused by the examining division.

VI. On 13 October 2014 the board issued a summons to attend oral proceedings on 31 March 2015.

VII. In a phone conversation held on 16 March 2015 the rapporteur informed the appellant's representative of the board's intention to remit the case to the examining division with the order to grant a patent on the basis of the set of claims submitted by the appellant on 20 April 2011. With letter dated 17 March 2015 the appellant withdrew his request for oral proceedings. The board informed the appellant by letter of 23 March 2015 that the oral proceedings scheduled for 31 March 2015 were cancelled.

VIII. In his submissions of 20 April 2011, the appellant essentially argued that document D1 related to controlled release formulations which could contain baclofen as active ingredient. There was however no disclosure in D1 about the formulations being used in the treatment of spasticity. Accordingly, the subject-matter claimed was novel over D1. As to inventive step, he remarked that on the basis of the prior art available at the time the application was filed, the skilled person would have considered baclofen as completely unsuitable for a controlled-release system. It was therefore surprising to find that the formulations disclosed in D1 provided an efficacy in spasticity over a 24-hour period while providing lower levels of sedation. Hence, the subject-matter of claim 1 met the requirements of Article 56 EPC.

IX. The appellant requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request filed with letter dated 20 April 2011.

Reasons for the Decision

Main request

1. Article 123(2) EPC

1.1 The application as originally filed contained four claims drafted in accordance with the Swiss-type format. In the main request the original claims have been reworded in the form of purpose-restricted composition claims according to Article 54(5) EPC. This modification does not involve any addition of subject-matter and therefore complies with the requirements of Article 123(2) EPC.

1.2 Further amendments introduced in claim 1 concern the indication that the baclofen composition is for oral administration and that it is used in the treatment of spasticity.

The feature relating to oral administration finds support for instance on page 1, lines 2 to 4, of the original application.

As to the indication that the composition is used in the treatment of spasticity, it is noted that original claim 1 defined the group of patients ("human patients suffering from signs and symptoms of spasticity") without providing an explicit indication of the clinical condition treated. This could however be derived from the application as a whole and in particular from page 4, lines 5 to 9, and page 5, fourth paragraph.

The requirements of Article 123(2) EPC are therefore met.

2. Article 54 EPC

As discussed above, claim 1 is worded in the form of a purpose-restricted composition claim according to Article 54(5) EPC. More specifically, it relates to an oral controlled-release formulation containing baclofen for use in the treatment of spasticity.

2.1 Document D1 relates to a gastric-retention controlled-release composition comprising a controlled-release core and a rapidly releasing coating (paragraphs [0024] to [0026]). The active ingredient can be selected among various substances which are grouped according to their mechanism of action or their therapeutic application (paragraphs [0027] to [0070]). Paragraph [0060] provides examples of drugs belonging to the class of muscle relaxants and specifically mentions baclofen. Examples 1 to 3 disclose the preparation of controlled-release compositions containing baclofen. Example 4 relates to a study of pharmacokinetics in which healthy male volunteers received once a day the baclofen formulation of example 2 (see [0100] to [0101]).

2.2 Neither paragraph [0060] nor examples 1 to 4 or any other passage of document D1 disclose a therapeutic application for the baclofen composition or for other compositions containing a muscle relaxant. In particular, nowhere in D1 is it mentioned that compositions containing baclofen can be used in the treatment of spasticity.

2.3 In its decision the examining division observed that "muscle relaxants are useful in the treatment of muscle stiffness, which is a well-known sign of spasticity".

However, there is no indication in the prior art that muscle relaxants and in particular baclofen are to be used exclusively in the treatment of spasticity. For

instance, it is stated in document D2 that baclofen can be used in the treatment of spasticity in view of its effect on the reduction of muscle tone. However, it is explained in the same document that in addition to this application it can also be used e.g. in controlling gastro-esophageal reflux disease, promoting alcohol abstinence, promoting smoking cessation, treatment of emesis and treatment of cough (see paragraph bridging pages 3 and 4). Furthermore, the board notes that some molecules mentioned in paragraph [0060] of document D1 as examples of muscle relaxant are also mentioned in other parts of document D1 as belonging to other categories of drugs. For instance, meprobamate is also included in the list of psychotherapeutic agents (see [0067]), and methocarbamol is also mentioned as an example of antispasmodic and anticholinergic agents (see [0044]). This means in the board's view that a muscle relaxant can also be used for therapeutic applications other than the treatment of spasticity. Therefore, the examining division's conclusion that D1 provides an implicit disclosure of the use of the baclofen compositions in the treatment of spasticity is not tenable.

2.4 From the above the board concludes that the subject-matter of claim 1 is novel over the disclosure of D1 at least on account of the use of the controlled drug delivery system in the treatment of spasticity (Article 54(1) and (5) EPC).

The requirement of novelty is therefore met.

3. Inventive step

3.1 The invention underlying the application relates to the use of baclofen formulations in the treatment of

spasticity (page 1, lines 1 to 4). More specifically, it addresses the problem of providing a treatment of spasticity which avoids the occurrence of the side effects normally caused by the oral administration of baclofen, in particular sedation and dizziness (page 2, first paragraph).

Closest prior art

3.2 In the board's opinion D1 and D4 are the most relevant documents to be considered in the context of selecting the closest prior art.

Document D1, which was selected as the closest prior art in the appealed decision, relates to controlled-release formulations that can contain baclofen as active ingredient (see point 2.1 above). The formulation disclosed in example 2 of this document is identical to the formulation disclosed in Table 4 of the present application. As discussed above, D1 does not address the problem of providing a treatment for spasticity. Nor is D1 concerned with the problem of avoiding or reducing the side effects associated with the use of baclofen. In more general terms, document D1 relates to aspects of galenics rather than pharmacology.

Document D4 relates to controlled-release pharmaceutical compositions for the treatment of spasticity which are suitable for intrathecal or epidural injection and can contain baclofen as active ingredient (see page 13, lines 17 to 27, and claims 23 and 24). It is explained in this document that conventional therapies for spasticity, based on the oral administration of baclofen, cause important side effects, in particular sleepiness (page 4, lines 4 to

9). The baclofen formulations disclosed in D4 provide various beneficial effects, including improved tolerance (page 8, line 25).

3.3 According to the established case law, in selecting the closest prior art, the first consideration is that it must be directed to the same purpose or effect as the invention (Case Law of the Boards of Appeal of the European Patent Office, 7th edition 2013, I.D.3.2).

The considerations set out in point 3.2 above show that while D4 is concerned with the same purpose as the present application, namely treating spasticity with a baclofen-based therapy whilst preventing the associated side effects, these objectives are ignored in D1.

Consequently, contrary to the examining division's view,
the board concludes that document D4 represents the closest prior art. As it appears from points 2.3 and 3.2 (second paragraph) above, the conclusion of the examining division that document D1 represented the closest prior art was based on a wrong assessment of the teaching of this document which led also to a different outcome on the issue of inventive step (see below).

Technical problem

3.4 The problem underlying the application in suit in the light of D4 can be seen in the provision of an alternative baclofen-based therapy for spasticity, wherein said therapy provides a low level of sedation.

3.5 As a solution to this problem the application proposes a controlled drug delivery system according to claim 1

which comprises an effective dose of baclofen and which is characterised *inter alia* in that it is administered orally once a day.

3.6 The application discloses in Tables 7 and 8 the results of a clinical study involving 90 patients with neurological spasticity. The patients were initially stabilised on conventional baclofen therapy, consisting in the administration of immediate-release tablets three times a day. This therapy was then replaced by a treatment according to the invention, consisting in the administration of controlled-release baclofen formulations once a day. The total amount of baclofen given in a day remained constant during the two phases of the experiment. Tables 7 and 8 show that the switch from the conventional therapy (i.e. immediate release) to the therapy according to the application in suit is associated with a significant decrease in the Ashworth rigidity score, used for grading the spasticity, and in the sedation score. The latter result clearly indicates the improved sedation profile of the therapy of the invention compared to conventional oral baclofen therapies.

In the light of these results the board is satisfied that the technical problem defined in point 3.4 above has been solved.

Obviousness

3.7 Document D4 clearly indicates that the oral administration of baclofen in amounts sufficient to be effective results in noteworthy side effects, in particular sleepiness (page 4, second paragraph). The same teaching can also be drawn from document D2, which states that "When baclofen is given orally, sedation is

a side effect, particularly at elevated doses." (page 4, lines 16 and 17). Thus, documents D2 and D4 would have discouraged the skilled person faced with the problem of providing a baclofen-based therapy for spasticity whilst preventing the associated problems of sedation from considering oral administration as a suitable option.

Nor would the teaching of D1 have modified his sceptical attitude towards this mode of administration. This document does indeed describe controlled-release tablets of baclofen to be administered once a day. However, it does not provide any information as to the issue of preventing or reducing the side effects associated with the oral administration of baclofen, in particular sedation. Thus, in the absence of any information in this respect the skilled person would have regarded the formulations disclosed in D1 as suffering the same drawbacks discussed in D4 and D2 in relation to oral baclofen formulations, and therefore not suitable for solving the technical problem.

Hence, the available prior art does not suggest that daily administration of an oral controlled-release formulation of baclofen would provide an effective treatment for spasticity without causing significant sedation.

3.8 On that basis claim 1 meets the requirements of Article 56 EPC.

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 with the order to grant a patent on the basis of the claims of the request submitted with letter dated 20 April 2011 and a description to be adapted thereto.

The Registrar: The Chairman:

S. Fabiani J. Riolo

Decision electronically authenticated