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Datasheet for the decision of 16 June 2009

Case Number: T 0200/07 - 3.3.02

Application Number: 02257582.3

Publication Number: 1310245

IPC: A61K 9/20

Language of the proceedings: EN

Title of invention:
Clopidogrel bisulfate tablet formulation

Patentee:
SHERMAN, Bernard Charles

Opponent:
NORTON HEALTHCARE LTD

Headword:
Clopidogrel bisulfate formulation/SHERMAN

Relevant legal provisions:
EPC Art. 54, 56, 114(2)

Relevant legal provisions (EPC 1973):
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Keyword:
"Introduction of lack of novelty as new ground of opposition (no): no approval of the patentee"
"Inventive step - (no): improvement obvious"

Decisions cited:
G 0010/91

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0200/07 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 16 June 2009

Appellant: (Opponent)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 23 November 2006 rejecting the opposition filed against European patent No. 1310245 pursuant to Article 102(2) EPC.

Composition of the Board:

Chairman: J. Riolo
Members: A. Lindner
C. Vallet

Summary of Facts and Submissions

I. European patent No. 1 310 245 based on application No. 02 257 582.3 was granted on the basis of a set of 10 claims.

The sole independent claim reads as follows:

"1. A pharmaceutical tablet which comprises clopidogrel bisulfate and a lubricant selected from the group consisting of zinc stearate, sodium stearyl fumarate and stearic acid."

II. An opposition was filed against the granted patent. The patent was opposed under Article 100(a) EPC for lack of inventive step and under Article 100(b) EPC for insufficient disclosure of the invention.

III. In his letter dated 18 July 2006, the opponent cited lack of novelty as a new ground of opposition (Article 100(a) EPC in conjunction with Article 54 EPC).

IV. The documents cited during the opposition and appeal proceedings included the following:

(1) Handbook of Pharmaceutical Excipients, 2nd ed., A. Wade and P.J. Weller (ed.), The Pharmaceutical Press, 1994

(3) US-A-5 006 344

(5) US-A-5 562 921

(6) US-A-5 520 928

(8) US-A-4 847 265

(10) Liebermann and Lachman (ed.): "Pharmaceutical Dosage Forms, Tablets" 1980, Marcel Dekker Inc., New York, Basel 1

(11) A.T. Florence (ed.): "Materials Used in Pharmaceutical Formulation" 1984, Blackwell Scientific Publications, Oxford

V. In the decision pronounced on 14 September 2006, the opposition division rejected the opposition. It did not admit lack of novelty into the proceedings, as this ground had been late-filed. Moreover, documents (8) and (11) had not been found to be *prima facie* pertinent for novelty. As regards sufficiency of disclosure, the opposition division essentially argued that the burden of proof was with the opponent, who, however, had not provided any evidence that the disclosure of the contested patent was insufficient. In connection with inventive step, the opposition division decided to admit late-filed documents (8) and (11) into the proceedings. The subject-matter of the contested patent was not rendered obvious by either the product PLAVIX™ or document (8), which could both be defined as closest prior art.

VI. The opponent (appellant) lodged an appeal against that decision.

VII. With his reply to the statement of the grounds of appeal dated 24 August 2007, the patentee (respondent) filed auxiliary requests 1 and 2. The independent claims read as follows:

(a) auxiliary request 1:

"1. A pharmaceutical tablet which comprises clopidogrel bisuflate and a lubricant selected from the group consisting of zinc stearate, sodium stearyl fumarate and stearic acid, wherein when the lubricant is stearic acid the amount of lubricant is from 1 to 6% by weight of the tablet."

(b) auxiliary request 2:

"1. A pharmaceutical tablet which comprises clopidogrel bisuflate and a lubricant selected from the group consisting of zinc stearate, sodium stearyl fumarate and stearic acid, wherein when the lubricant is zinc stearate or sodium stearyl fumarate the amount of lubricant is from 0.5 to 3% by weight of the tablet and when the lubricant is stearic acid the amount of lubricant is from 1 to 6% by weight of the tablet."

VIII. Oral proceedings took place on 16 June 2009.

IX. The appellant's arguments in connection with inventive step can be summarised as follows:

Either the product PLAVIX™ or document (8) could be defined as closest prior art. PLAVIX™ concerned tablets comprising clopidogrel bisulfate as active agent and hydrogenated castor oil and PEG 6000 as lubricants. As the contested patent did not contain any evidence that the lubricants used therein were superior to the lubricants of PLAVIX™, the problem underlying the present invention consisted in the provision of clopidogrel bisulfate tablets comprising

an alternative lubricant. The solution to that problem was obvious in view of the fact that the lubricating effect of stearic acid, zinc stearate and sodium stearyl fumarate was known from document (1). It was not contested that magnesium stearate would have been the first choice, but there the skilled person would have immediately observed stability problems with the active agent, and as a consequence passed on to other well known lubricants such as stearic acid, zinc stearate or sodium stearyl fumarate.

X. The respondent's arguments in connection with inventive step can be summarised as follows:

Document (8) rather than PLAVIX™ constituted the closest prior art in view of the higher structural similarity of magnesium stearate to the lubricants used in the contested patent. However, as regards PLAVIX™ as closest prior art, it was common general knowledge that PEG 6000 and hydrogenated castor oil were poor lubricants. As a consequence, the problem of the present invention concerned the provision of a clopidogrel bisulfate tablet composition comprising a lubricant with improved lubricating properties. The skilled person, trying to solve this problem, would have immediately chosen magnesium stearate as a replacement for PEG 6000 and hydrogenated castor oil. But there he would have been confronted with a new problem, as magnesium stearate promoted degradation of clopidogrel bisulfate. Surprisingly, this degradation did not occur with the lubricants of the present invention. There was no incentive in the prior art for the skilled person to select, out of the vast number of possible lubricants, the three compounds of the

present invention in order to avoid the stability problems of magnesium stearate on the one hand and to improve the lubricating performance as compared to PEG 6000 and hydrogenated castor oil on the other hand.

In connection with auxiliary requests 1 and 2, the respondent argued that the introduction of concentration ranges further delimited the claimed subject-matter from the prior art.

XI. The appellant requested that the decision under appeal be set aside and that the European patent No. 1310245 be revoked.

The respondent requested that the appeal be dismissed or that the patent be maintained in amended form on the basis of auxiliary requests 1 or 2, filed with letter dated 24 August 2007.

Reasons for the Decision

1. The appeal is admissible.

2. Admissibility of lack of novelty as new ground of opposition:

Lack of novelty as ground of opposition according to Article 100(a) EPC was first raised in the opponent's letter of 18 July 2006, i.e. after expiry of the opposition period defined by Article 99(1) EPC. The opposition division, making use of its discretion under Article 114(2) EPC, decided not to admit this ground of opposition into the proceedings, because the

objections which had been based on document (8) interpreted in the light of document (11) were not considered to be *prima facie* relevant (see point 3 of the reasons). The board has no reason to believe that the opposition division wrongly exercised its discretion, so lack of novelty forms a fresh ground for opposition which according to decision G 10/91 may be considered in appeal proceedings only with the approval of the patentee. Since the patentee did not give his approval, lack of novelty cannot be introduced into the appeal proceedings. The board moreover observes that the appellant did not contest that the opposition division had correctly exercised its discretion.

3. Sufficiency of disclosure:

The board agrees with the conclusions of the opposition division in connection with the sufficiency of disclosure (see point 2 of the decision of the opposition division). In view of the board's finding with regard to inventive step (see point 4 below), it is not necessary to further develop the ground of opposition raised under Article 100(b) EPC.

4. Inventive step:

4.1 Main request:

4.1.1 The subject-matter of the main request concerns stable clopidogrel bisulfate tablets comprising a lubricant selected from zinc stearate, sodium stearyl fumarate and stearic acid (see paragraph [0009] of the contested patent).

4.1.2 The product PLAVIX™ relates to tablets comprising clopidogrel bisulfate, lactose, microcrystalline cellulose, pregelatinised starch, hydrogenated castor oil and PEG 6000 (see paragraphs [0002] and [0003] of the contested patent and document (16)). The latter two compounds were added as lubricants. The board considers that PLAVIX™ can be defined as closest prior art.

4.1.3 The respondent argued that it was common general knowledge that PEG 6000 and hydrogenated castor oil were poor lubricants. This fact was confirmed by the appellant. As a consequence, the problem underlying the invention as defined in the main request can be seen in the provision of a clopidogrel bisulfate tablet comprising a lubricant with improved lubricating properties. The problem was solved by the replacement of hydrogenated castor oil and PEG 6000 by zinc stearate, sodium stearyl fumarate and stearic acid.

4.1.4 Despite the fact that the respondent did not submit any evidence for the improved lubricating properties of zinc stearate, sodium stearyl fumarate and stearic acid as compared to the lubricants of PLAVIX™, the board is convinced that the above-mentioned problem was solved, as the poor lubricating performance of the PEG 6000 and hydrogenated castor oil is common general knowledge (see points IX and X above). On the other hand, the lubricating properties of zinc stearate, sodium stearyl fumarate and stearic acid were well known at the priority date of the contested patent (see document (1), paragraph "Functional Category" on

pages 569, 467 and 494). Moreover, stearic acid was known to be an efficient lubricant, while zinc stearate was characterised by excellent lubricating properties (see document (10), page 130, first sentence of the last paragraph and p. 131, penultimate paragraph). As a consequence, the skilled person was aware that substitution of a lubricant as claimed in the present main request for PEG 6000 and hydrogenated castor oil would improve the lubricating performance. It is therefore not necessary to prove this effect by experimental evidence. However, a further consequence is that, this effect being obvious for the skilled person, the replacement of the lubricants of PLAVIX™ by any one of zinc stearate, sodium stearyl fumarate or stearic acid cannot establish an inventive step. Therefore, the requirements of Article 56 EPC are not met.

4.1.5 Further arguments of the respondent:

4.1.5.1 The skilled person, trying to solve the problem defined in point 4.1.3 above, would immediately turn to magnesium stearate, which was the lubricant of choice. But there he would discover the interaction of magnesium stearate with clopidogrel bisulfate which caused degradation of the active agent. The skilled person would expect that the same problems would occur with the structurally similar compounds zinc stearate, sodium stearyl fumarate or stearic acid and therefore immediately dismiss these lubricants.

It is not denied that magnesium stearate is the lubricant of choice. However, this does not mean that it is universally applicable. It follows from the

prior art that magnesium stearate is incompatible with certain active agents (see document (11), paragraph bridging pages 130 and 131, see also documents (3), (5) and (6). If such an incompatibility with magnesium stearate occurs the skilled person would simply try another known lubricant such as stearic acid. As a consequence, this argument cannot succeed.

4.1.5.2 The respondent also reasoned that there was no pointer in the prior art to select zinc stearate, sodium stearyl fumarate or stearic acid out of the large list of lubricants.

Again reference is made to document (10), which describes lubricants such as stearates including magnesium, calcium and zinc stearate as well as stearic acid. There, the excellent lubricating properties of zinc stearate are mentioned as well as the fact that stearic acid is an efficient lubricant (see page 130, first sentence of the last paragraph and p. 131, penultimate paragraph). As a consequence, the skilled person had an incentive to select these lubricants in order to solve the problem as defined in point 4.1.3 above.

4.1.6 In order to meet the requirements of Article 56 EPC, an invention must involve an inventive step vis-à-vis each item of the prior art. As the subject-matter of the main request lacks an inventive step over PLAVIX™, it is not necessary to additionally assess inventive step starting from document (8) as closest prior art as proposed by the respondent. Such an additional assessment would not affect the above conclusions.

It is additionally noted that the passage in column 12, lines 3-11 of document (8) concerns tablets comprising *inter alia* an active ingredient and magnesium stearate. The active ingredient may be selected from various salts of clopidogrel such as the hydrochloride, the hydrobromide, the hydrogensulfate and the taurochlorate (see claims 2 to 5). As a consequence, document (8) does not specifically disclose tablets comprising clopidogrel hydrogensulfate plus Mg-stearate and is therefore not closer to the present invention than PLAVIX™.

4.2 Auxiliary request 1:

Claim 1 of auxiliary request 1 differs from claim 1 of the main request by the introduction of a concentration range of 1 to 6% by weight for stearic acid. However, these concentrations are usual for stearic acid. Thus, document (1) (see table on page 494) discloses a concentration of 1-3% for stearic acid when it is used as a tablet lubricant. No changes were made with regard to zinc stearate and sodium stearyl fumarate. As a consequence, the reasoning developed in point 4.1 for the main request applies *mutatis mutandis* to claim 1 of auxiliary request 1. The requirements of Article 56 EPC are therefore not met.

4.3 Auxiliary request 2:

Claim 1 of auxiliary request 2 differs from claim 1 of the main request by the introduction of a concentration range of 1 to 6% by weight for stearic acid and of 0.5 to 3% by weight for zinc stearate and

sodium stearyl fumarate. As regards the concentration range for stearic acid, see point 4.2 above. With respect to the concentration range of 0.5 to 3%, it is noted that this is a usual range for zinc stearate and sodium stearyl fumarate (see document (1), page 467, middle of the left-hand column, which cites a concentration range of 0.5 to 2.0% by weight for sodium stearyl fumarate, and page 569, where a concentration of up to 1.5% by weight is defined for zinc stearate). As a consequence, the reasoning developed in point 4.1 for the main request applies *mutatis mutandis* to claim 1 of auxiliary request 2. The requirements of Article 56 EPC are therefore not met.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

N. Maslin J. Riolo