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D E C I S I O N
of 22 October 2003

Case Number: T 1048/99 - 3.3.2

Application Number: 88200396.5

Publication Number: 0282131

IPC: A61K 31/415

Language of the proceedings: EN

Title of invention:
Compositions and methods for treating gastrointestinal disorders

Patentee:
THE PROCTER & GAMBLE COMPANY

Opponent:
-

Headword:
Compositions for gastrointestinal disorders/THE PROCTER & GAMBLE COMPANY

Relevant legal provisions:
EPC Art. 56

Keyword:
"Main request and auxiliary requests 1, 2, 3, 6 and 7 - inventive step - no: incentive to try
Auxiliary requests 4, 5 - admissibility - no: late filed"

Decisions cited:
-

Catchword:
-

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Case Number: T 1048/99 **-** 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 22 October 2003

Appellant: (Proprietor of the patent)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 20 September 1999 revoking European patent No. 0282131 pursuant to Article 102(1) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: J. Riolo
J. Willems

Summary of Facts and Submissions

I. European patent No. 0 282 131, based on application No. 88 200 396.5, was granted on the basis of 12 claims.

Independent claims 1 and 6 as granted read as follows:

"1. Pharmaceutical compositions useful for treating or preventing gastrointestinal disorders, said compositions comprising:
a) a campylobacter-inhibiting antimicrobial agent;
b) an H_2 receptor blocking anti-secretory agent; and
c) a pharmaceutically-acceptable carrier."

"6. The use of a campylobacter-inhibiting antimicrobial agent and an H_2 receptor blocking anti-secretory agent for the manufacture of a medicament for the treatment or prevention of gastrointestinal disorders selected from non-ulcerative gastrointestinal disorders such as chronic or atrophic gastritis, non-ulcer dyspepsia, esophageal reflux disease, gastric motility disorders and peptic ulcer disease, selected from gastric, duodenal and jejunal ulcers, in humans or lower animals, said treatment or prevention comprising administering to said human or lower animal a composition comprising, by weight, from 0.1% to 99.8% of the campylobacter-inhibiting antimicrobial agent and concurrently administering to said human or lower animal a safe and effective amount of an H_2 receptor blocking anti-secretory agent."

II. Oppositions were filed against the granted patent by opponent O1, respondent 2 (opponent O2), respondent 3 (opponent O3) and opponent 4. The patent was opposed

under Article 100(a) EPC for lack of novelty and inventive step and because it lacked industrial applicability under Article 52(4), and under Article 100(b) EPC for insufficiency of disclosure.

With its letter dated 18 December 1996, opponent O1 withdrew its opposition.

The following documents were cited *inter alia* during the proceedings before the Opposition Division and the Board of Appeal:

(3) DMW, 1986, 111. Jg., Nr. 38, pages 1459 to 1461

(5) British Medical Journal, 1976, 2, pages 686 to 688

(27) Lyon's declaration filed with letter dated 11 November 1998.

III. By its decision pronounced on 14 December 1998, the Opposition Division revoked the patent under Article 102(1) EPC.

The Opposition Division held that the patent in suit did not meet the requirements of inventive step.

In its opinion, the subject-matter of the contested patent was novel over the prior art because the prior art described neither compositions containing a mixture of (a) an antimicrobial agent, (b) an H_2 receptor blocking anti-secretory agent cimetidine and (c) a pharmaceutically-acceptable carrier, nor that the constituents (a) and (b) were administered concurrently.

As to inventive step, the Opposition Division regarded document (3) as representing the closest state of the art. In its opinion the only distinguishing feature over said disclosure was the concurrent administration of the antimicrobial agent (a) and the H_2 receptor blocking anti-secretory agent cimetidine (b). Since, in its opinion, no effect was plausibly demonstrated for this particular regimen, it considered that the subject-matter of the patent in suit lacked inventive step. In its view, the new regimen amounted merely to an obvious simplification of the administration which was in fact a reasonable and desirable objective that the skilled person would in any case seek to achieve.

IV. The appellant (patentee) lodged an appeal against the said decision.

V. Oral proceedings were held before the Board on 22 October 2003.

The appellant filed seven auxiliary requests during the appeal proceedings.

Claim 1 of the main request filed on 28 January 2000 and of the first auxiliary request filed during the oral proceedings read:

"1. Pharmaceutical compositions useful for treating or preventing gastrointestinal disorders, said compositions comprising:
a) a campylobacter-inhibiting antimicrobial agent **selected from antibiotics**;
b) an H_2 receptor blocking anti-secretory agent; and

c) a pharmaceutically-acceptable carrier." (Emphasis added)

Claim 1 of the second, third and sixth auxiliary requests read:

"1. Pharmaceutical compositions useful for treating or preventing gastrointestinal disorders, said compositions comprising:
a) a campylobacter-inhibiting antimicrobial agent **selected from antibiotics**;
b) an H_2 receptor blocking anti-secretory agent **which is ranitidine**; and
c) a pharmaceutically-acceptable carrier." (Emphasis added)

Claim 1 of the seventh auxiliary request reads:

"1. The use of a campylobacter-inhibiting antimicrobial agent **selected from antibiotics** and an H_2 receptor blocking anti-secretory agent **which is ranitidine** for the manufacture of a medicament for the treatment or prevention of gastrointestinal disorders selected from non-ulcerative gastrointestinal disorders such as chronic or atrophic gastritis, non-ulcer dyspepsia, esophageal reflux disease, gastric motility disorders and peptic ulcer disease, selected from gastric, duodenal and jejunal ulcers, in humans or lower animals, said treatment or prevention comprising administering to said human or lower animal a composition comprising, by weight, from 0.1% to 99.8% of the campylobacter-inhibiting antimicrobial agent and a safe and effective amount of an H_2 receptor blocking anti-secretory agent, **wherein the campylobacter-**

inhibiting antimicrobial agent and the H_2 receptor blocking antisecretory agent are administered within 5 minutes of each other." (Emphasis added).

VI. The appellant mainly argued that, having regard to the comparative experiments in document (27), the problem to be solved over the closest prior art, ie document (3), was the provision of a formulation having improved efficacy. As, in its opinion, the available prior art was silent about any link between concurrent administration of the two drugs and improvement of efficacy of the treatment, it considered that the subject-matter of the contested patent involved an inventive step.

In addition, it also submitted that, even if the problem to be solved was merely the improvement of patient compliance, the solution provided by the patent in suit implied an inventive step.

In fact, in its view, as the skilled person would not consider administering both drugs concurrently with a reasonable expectation of success, he would not even try it.

VII. Respondents 3 and 4 filed no submissions during the appeal proceedings and they did not attend the oral proceedings.

With its letter dated 28 July 2003, opponent O4 withdrew its opposition.

VIII. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the

basis of the main request filed on 28 January 2000 or, alternatively, on the basis of the auxiliary requests 1 to 7 filed during the oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. *Admissibility of auxiliary requests 4 and 5.*

Contrary to the other auxiliary requests filed during the oral proceedings which were amended by introducing either features from dependent claims or features which were already proposed as amendments during the written procedure (appellant's letter dated 28 January 2000, point 2.6), independent claim 6 of these sets of claims contains a feature from the description of the patent in suit relating to the reduction of relapse rate.

In that respect, the Board observes that, in reply to the question why these requests had not been filed earlier, no justification at all was provided.

The Board notes also that, as a rule, in the absence of particular circumstances, the missing parties could not expect a feature of the description to be introduced in the claims. No such circumstances were submitted by the appellant in the present case.

Accordingly, the Board judges that these requests cannot be admitted into the procedure as late-filed.

3. *Main request and first auxiliary request*

Inventive step

3.1 The subject-matter of the contested patent relates to pharmaceutical compositions useful for preventing gastrointestinal disorders, comprising a campylobacter-inhibiting antibiotic and an histamine-2 receptor blocking anti-secretory agent (page 2, lines 3 to 4, page 3, lines 55 to 57).

According to the description of the contested patent, the two agents are co-administered by administering a composition according to claim 1 (page 10, lines 34 to 36).

The Board considers that document (3), which also concerns a treatment for preventing gastrointestinal disorders, comprising administration of a campylobacter-inhibiting antibiotic (Ofloxacin, Tarivid® tablet) and an histamine-2 receptor blocking anti-secretory agent (ranitidine, Zantic® tablet), represents the closest state of the art (page 1460, middle column, lines 22 to 39).

This document discloses a treatment of 4 patients with 300 mg ranitidine at night and 200 mg ofloxacin twice daily (table 1).

As to the evidence on file (27) which is intended demonstrate that an effect is achieved by the claimed formulation over this closest prior art item, the Board observes that the experiments are carried out on guinea pigs and that intramuscular ranitidine administration followed immediately by oral administration of

ofloxacin is compared with oral administration of ofloxacin followed by intramuscular ranitidine administration given four hours later.

The Board is not convinced that this is a valid comparison of the subject-matter of claim 1 with the closest state of the art embodiment according to document (3).

In fact, in document (3) the experiments were carried out on humans and the two drugs were taken orally for at least 14 days. Moreover, according to claim 1, the two drugs are present in a composition as a mixture, so that they cannot be administered the one orally and the other intramuscularly.

Accordingly, no plausible effect can be recognised for the administration of the present composition in the treatment of gastrointestinal disorders vis-à-vis the closest prior art.

In that respect, the appellant declared during the oral proceedings that, according to the scientist who carried out the experiment, the results would have been even better if the comparison had been carried out adequately.

Such a declaration needs, however, to be substantiated by further evidence, in particular in the absence of the other parties.

3.2 Accordingly, the Board agrees with the Opposition Division's view that the problem to be solved by the subject-matter of claim 1 of the main request of the

patent in suit as against document (3) can only be seen in the provision of a formulation improving patient compliance.

3.3 This problem is solved by the subject-matter of claim 1, ie by the use of a pharmaceutical composition comprising both drugs. In the light of the description of the patent in suit, the Board is satisfied that the problem has been plausibly solved.

3.4 Thus the question to be answered is whether the proposed solution, ie providing a formulation containing an antibiotic and an H_2 receptor blocking anti-secretory agent as a composition, would have been obvious to the skilled person in the light of the prior art.

In that respect, document (5), which concerns a study on deviation from prescribed drug treatment after discharge from hospital, clearly teaches that "adherence to drug treatment is unlikely to be improved unless doctors attempt to make their patient's regimens as simple as possible; in this context the use of combined drug preparations may have benefits that outweigh their theoretical disadvantages." (page 688, left column, "Discussion", third paragraph, last sentence).

Accordingly, the Board is satisfied that the skilled person faced with the problem as defined above under 3.3 would be prompted to use both drugs in a single composition, just by following the teaching of document (5).

3.5 The Board does not agree with the appellant's contention, as part of its main argument, that the claimed formulation is inventive because the skilled person would not expect the use of both drugs in a single pharmaceutical preparation to be successful, so that he would not even try it.

It is indeed true, as pointed out by the appellant during the oral proceedings, that document (5) is a very general document, which does not mention the two drugs according to the patent in suit, and that its teaching is very broad.

It is also true that attention must be paid to possible interaction between the two drugs when they are taken together and that a study in that respect needs to be carried out first in order to determine whether a concurrent administration is acceptable.

However, in the absence of any element demonstrating that there is a technical prejudice in the art against the concomitant use of an antibiotic and an H_2 receptor blocking anti-secretory agent or at least that the overcoming of particular difficulties would be required for the preparation and the testing of such a formulation, the Board concludes that, having regard to the importance of patient compliance with the prescribed regiment, it is of minor significance whether or not a particularly high degree of success was expected before starting experimental work. Therefore the Board is convinced that the skilled person would in any case have tried to prepare a formulation containing both drugs in a composition.

3.6 In the light of these facts, the Board can only conclude that the subject-matter of claim 1 of the main request does not involve an inventive step as required by Article 56 EPC.

Under these circumstances, there is also no need to consider the remaining claims of the main request.

As claim 1 of the first auxiliary request is identical to claim 1 of the main request, these conclusions hold good for this set of claims as well.

4. *Auxiliary requests 2, 3 and 6.*

These requests differ from the main request in that the medicament is now restricted to ranitidine as an H_2 receptor blocking anti-secretory agent.

The appellant argued that the submissions presented with respect to inventive step remained valid for these sets of claims as well.

The Board notes that this restriction adds in fact no new distinguishing feature vis-à-vis the closest prior art (3) which also deals with ranitidine.

As no further argument has been presented as to why this restriction should involve an inventive step, the conclusions under 3.6 hold good for these requests as well.

5. *Auxiliary request 7*

As discussed during oral proceedings, claim 1 is drafted as a second medical use claim, which encompasses a composition according to claim 1 of 2, 3 and 6 auxiliary requests in the treatment of gastrointestinal disorders.

This request also differs from these requests in that the medicament is now restricted to the treatment of selected gatrointestinal disorders, a drug range within 0.1% and 99.8% by weight and the fact that the two drugs might be taken either as a mixture or administered separately within 5 minutes of each other.

The Board notes that, as far as the drugs mixture is concerned, these restrictions add in fact no new distinguishing feature vis-à-vis the closest prior art (3), which deals with the same gastrointestinal disorders (ie *Ulcus duodeni*, *Ulcus ventriculi*) and the same drug range.

As apparent from points 3 and 4 of the decision, the drugs mixture lacks an inventive step for these medical indications.

Accordingly, the subject-matter of claim 1 of auxiliary request 7 does not fulfil the requirement of inventive step either.

As pointed out during the oral proceedings, there is therefore no need to discuss the other embodiments covered by claim 1 either as to novelty or as to inventive step.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Townend U. Oswald