BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [ ] To Chairmen and Members
(C) [X] To Chairmen

D E C I S I O N
of 20 July 2000

Case Number: T 0229/97 - 3.3.1

Application Number: 90113986.5

Publication Number: 0409281

IPC: C07D 207/327

Language of the proceedings: EN

Title of invention:
(R-(R*R*))-2-(4-fluorophenyl)-beta, delta-dihydroxy-5-(-1-methylethyl-3-phenyl-4((phenylamino)-carbonyl)-1H-pyrrole-1-heptanoic acid, its lactone form and salts thereof

Applicant:
WARNER-LAMBERT COMPANY

Opponent:
-

Headword:
Atorvastatin/WARNER-LAMBERT

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

Keyword:
"Inventive step (yes, after amendment) - proper comparison - unexpectedly improved handling"

Decisions cited:
-

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0229/97 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 20 July 2000

Appellant: WARNER-LAMBERT COMPANY
201 Tabor Road
Morris Plains
New Jersey 07950 (US)

Representative: Henkel, Feiler, Hänzel
Möhlstrasse 37
D-81675 München (DE)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 5 September 1996 refusing European patent application No. 90 113 986.5 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: A. J. Nuss
Members: R. Freimuth
R. T. Menapace

Summary of Facts and Submissions

I. The appeal lodged on 29 October 1996 lies from the decision of the Examining Division posted on 5 September 1996 refusing European patent application No. 90 113 986.5 (European publication No. 409 281).

II. The decision under appeal was based on claims 1 to 13 as originally filed. The Examining Division found that the subject-matter of the claims lacked inventive step based on the document

(1) US-A-4 681 893,

disclosing the trans- and (R*R*)-racemic mixtures of the claimed enantiomers, respectively, to be used as hypocholesterolemic agents.

The Examining Division held that the person skilled in the art would have expected that one of both enantiomers, resulting from splitting the racemic mixtures of document (1), exhibited a higher hypocholesterolemic activity than the racemic mixture. The extent of that expected increase in activity was not to be regarded as an indication of inventive step.

III. In a communication pursuant to Article 11(2) of the rules of procedure of the Boards of Appeal, the Board casted doubts on whether the extent of an expected increase of that activity could be considered as an indication of inventive step.

IV. At the Oral proceedings before the Board, held on 20 July 2000, the Appellant (Applicant) submitted fresh claims 1 to 4 and an adapted description, claim 1

reading as follows:

"1. The hemicalcium salt of [R-(R*,R*)]-2-(4-fluorophenyl)-â,ä-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)-carbonyl]-1H-pyrrole-1-heptanoic acid."

Claim 2 was directed to a pharmaceutical composition comprising the compound of claim 1, claim 3 to the use of that compound for the preparation of a pharmaceutical composition and claim 4 to a process for the preparation of that compound.

The Appellant argued that those claims were restricted to subject-matter involving an inventive step. He submitted that the problem underlying the application was to be seen in providing a further hypocholesterolemic compound with improved handling properties, in particular hygroscopicity and solubility. To back up his submission, the Appellant filed on 20 June 2000 an experimental report which showed the superiority of the claimed hemicalcium enantiomer over the sodium racemate of example 2 of the closest prior art document (1) with respect to hygroscopicity and solubility. The improvement in both handling properties was surprising, thereby supporting inventive step.

V. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of claims 1 to 4 and the description pages 1 to 20 as submitted during oral proceedings.

VI. At the end of the oral proceedings the decision of the Board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Amendments (Article 123(2) EPC)*

The subject-matter of claim 1 is based on claim 2 of the application as filed whereby the limitation of that claim to the hemicalcium salt is supported by original claim 6. Claims 2 to 4 are backed up by claims 11, 12 and 13 in combination with claim 6 of the application as filed.

For these reasons, the Board concludes that the claims as amended comply with the requirements of Article 123 (2) EPC.

3. *Novelty*

The Board is also satisfied that the subject-matter of the claims which refers to the hemicalcium salt of a particular enantiomer as defined in point IV above, meets the requirements of Article 54 EPC as already acknowledged by the Examining Division since document (1) specifically discloses only a salt of the corresponding racemate using a different cation.

4. *Inventive step*

It remains to decide whether or not the subject-matter of the present claims involves an inventive step as required by Article 56 EPC.

4.1 Claim 1 of the present application is directed to the

hemicalcium salt of a particular R-enantiomer of a 4-carboxamido substituted â,ä-dihydroxy-1H-pyrrole-1-heptanoic acid showing hypocholesterolemic activity. Document (1) which is the state of the art acknowledged in the application as filed on page 1, line 10, refers to similar compounds having the identical hypocholesterolemic activity (column 7, line 33), notably the sodium salt of the racemate of the claimed enantiomer (example 2).

The Board considers, in agreement with the Appellant and the Examining Division, that this disclosure of document (1) represents the closest state of the art and, hence, takes it as the starting point when assessing inventive step.

4.2 In view of this state of the art, the problem underlying the present application as submitted by the Appellant consists in providing a hypocholesterolemic compound having **improved** handling properties, in particular improved hygroscopicity and solubility.

4.3 As a solution to this problem the present application proposes the hemicalcium salt of the particular R-enantiomer as defined in claim 1.

4.4 To support his submission that the alleged improvement is achieved by the claimed invention, the Appellant referred to his experimental report filed on 20 June 2000. That test report comprises experimental data about the hygroscopicity and the solubility of the hemicalcium salt of the R-enantiomer according to the claimed invention, on the one hand, and of the sodium salt of the racemate of that enantiomer according to example 2 of document (1), on the other. Therefore, the

comparison of the experimental data for both compounds indicated in that test report truly reflects the achievements of the solution proposed by the claimed invention over the closest prior art. This specific comparison of both compounds is, thus, a fair basis for the assessment of inventive step.

Following that test report, the hemicalcium salt of the enantiomer according to the invention stored at the relative humidity of 53% shows a weight gain, i.e. a moisture adsorption, of 3.5% after 24 hours and of 3.8% after 14 days. The comparative sodium salt of the racemate according to document (1), however, shows under the same conditions a weight gain of 10.4% and of 10.6%, respectively. The significantly smaller amount of water uptake of the hemicalcium enantiomer compared to that of the sodium racemate demonstrates the lower hygroscopicity of the former. Therefore, the Appellant's test report evidences that the claimed hemicalcium salt of the enantiomer is superior in hygroscopicity to the comparative sodium salt of the racemate.

With respect to solubility, that test report shows that the sodium racemate according to document (1) yields in water and in neutral buffer an unacceptable gel which cannot be broken through filtration or centrifugation, whereas this phenomenon was not observed with the hemicalcium enantiomer according to the invention. Therefore, the Appellant's test report evidences that the solubility of the claimed hemicalcium salt of the enantiomer is improved over that of the comparative sodium salt of the racemate.

To summarize, the experimental data of that test report

with respect to hygroscopicity and solubility, hence, support the Appellant's submission that the hemicalcium salt of the enantiomer according to claim 1 has improved handling properties compared to the closest prior art document (1). For these reasons, the Board is satisfied that the problem underlying the patent in suit as defined in point 4.2 above is successfully solved by the claimed subject-matter.

4.5 Finally, it remains to be decided whether or not the proposed solution to the problem underlying the patent in suit involves an inventive step.

Document (1), i.e. the closest prior art document (see point 4.1 above), is directed *inter alia* to pharmaceutically acceptable salts of the racemates of 4-carboxamido substituted â,ä-dihydroxy-1H-pyrrole-1-heptanoic acids having hypocholesterolemic activity. However, that document does not address the problem underlying the present application of improving the handling properties, in particular hygroscopicity and solubility, of hypocholesterolemic compounds. Thus, document (1) neither gives any hint on how to solve that problem nor any incentive to modify those salts of the racemates into the hemicalcium salt of the particular R-enantiomer as defined in claim 1 in order to improve the handling properties thereof. Thus, document (1) does not point to the claimed solution proposed for solving the problem underlying the present application.

4.6 The Examining Division not relying on further documents in the decision under appeal in order to support his objection of obviousness, the Board, being not aware of any further relevant document, is, thus, satisfied that

the state of the art addressed in the proceedings does not render the claimed invention obvious.

4.7 For these reasons, the Board concludes that the subject-matter of claim 1, and by the same token that of independent claim 2, referring to a pharmaceutical composition comprising the compound as defined in claim 1, of independent claim 3, referring to the use of the compound as defined in claim 1 for the preparation of a pharmaceutical composition, and of independent claim 4, referring to a process for preparing the compound as defined in claim 1 involve an inventive step within the meaning of Articles 52(1) and 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 first instance with the order to grant a patent on the basis of the description pages 1 to 20 and the claims 1 to 4, both as submitted during the oral proceedings on 20 July 2000.

The Registrar: The Chairman:

N. Maslin A. Nuss