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Datasheet for the decision of 13 March 2012

Case Number: T 1170/07 - 3.3.02

Application Number: 98908008.0

Publication Number: 1017408

IPC: A61K 31/365, A61P 3/10

Language of the proceedings: EN

Title of invention:
Use of tethrahydrolipstatin in the treatment of diabetes type II

Patentee:
F. Hoffmann-La Roche AG

Opponent:
Ratiopharm GmbH

Headword:
Tethrahydrolipstatin for treating NIDDM/F. HOFFMANN-LA ROCHE AG

Relevant legal provisions:
EPC Art. 123(2), 113(1)
EPC R. 103

Keyword:
-

Decisions cited:
G 0002/10, T 0468/99, T 0246/08

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1170/07 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 13 March 2012

Appellant: (Opponent)
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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 14 May 2007 concerning maintenance of European patent No. 1017408 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: A. Lindner
L. Bühler

Summary of Facts and Submissions

I. European patent No. 1 017 408 based on application No. 98 908 008.0 was granted on the basis of 11 claims. The sole independent claim reads as follows:

"1. The use of tetrahydrolipstatin for the manufacture of an oral pharmaceutical preparation for treating type II diabetes mellitus per se, the amount of tetrahydrolipstatin to be employed in unit dosage form, which consists essentially of tetrahydrolipstatin formulated as an oral composition, the amount of tetrahydrolipstatin being effective to alleviate or cure type II diabetes mellitus per se and in the range of from 60 to 720 mg of tetrahydrolipstatin per day."

II. An opposition was filed against the patent. The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step and for non-patentability under Article 52(4) EPC, under Article 100(b) EPC for insufficiency of disclosure and under Article 100(c) EPC for amendments that contained subject-matter extending beyond the content of the parent application as filed.

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

(4) EP-A-0 638 317

(11) A.J. Scheen, et al., Diabete Metab. (1993), 19, 547-559

(13) R.R. Wing, et al., Arch. Intern. Med. (1987), vol. 147, 1749-1753

IV. The appeal lies from an interlocutory decision of the opposition division pronounced on 3 May 2007 and posted on 14 May 2007 maintaining the patent on the basis of the claims as granted and a description amended in the course of the opposition proceedings.

V. In said decision the opposition division decided that the ground for opposition under Article 100(c) EPC did not prejudice the maintenance of the patent in the form of the claims as granted, as the original application made it clear that the intended treatment concerned NIDDM (non-insulin dependent diabetes mellitus = type II diabetes mellitus) itself rather than potential risk factors thereof, so that the feature "type II diabetes mellitus per se" had a basis in the original application. Nor did the introduction of the unit dosage and the replacement of "comprising" by "consisting essentially of", which was introduced in order to exclude the presence of further active agents, prejudice the maintenance of the contested patent under Article 100(c) EPC.

Furthermore, the opposition division concluded that the priority was validly claimed and that the claimed subject-matter was not excluded from patentability by Article 52(4) EPC 1973. The claimed subject-matter was considered novel, as document (4) concerned improvement or elimination of the risk factors of NIDDM rather than its treatment per se.

Regarding inventive step, the opposition division defined the finding of alternative ways of improving NIDDM as the problem to be solved vis-à-vis document (13), the solution of which in the form of the

use according to claim 1 as granted was not rendered obvious by any of the available prior-art documents. Making reference to Article 69 EPC, the opposition division concluded that the amendment of the description as sole amendment was allowable under Rule 57(a) EPC 1973.

The decision under appeal does not, however, contain any reasoning as to why the invention according to the claims as granted is sufficiently disclosed.

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

VII. In the annex to the summons to oral proceedings pursuant to Article 15(1) RPBA, the board gave its preliminary opinion in connection with the ground for opposition under Article 100(c) EPC and the reimbursement of the appeal fee according to Rule 103(1)(a) EPC. According to this preliminary opinion, neither of the features "type II diabetes mellitus per se" and "60 to 720 mg of tetrahydrolipstatin per day" had a basis in the original application.

VIII. In a letter dated 9 February 2012, the respondent submitted arguments against the objections raised by the board in the annex to the summons to oral proceedings and filed auxiliary requests I to III.

IX. With a further letter dated 8 March 2012, the respondent submitted a main request and an auxiliary request I (corresponding to auxiliary requests II and III filed with letter dated 9 February 2012).

X. The appellant informed the board with a letter dated 29 February 2012 that it would not be attending the oral proceedings scheduled for 13 March 2012.

XI. Oral proceedings were held before the board on 13 March 2012. In the course of the oral proceedings, the respondent filed auxiliary requests II and III.

XII. The independent claims of the requests on file read as follows:

(i) Main request:

"1. The use of tetrahydrolipstatin for the manufacture of an oral pharmaceutical preparation for treating type II diabetes mellitus per se, the amount of tetrahydrolipstatin to be employed in unit dosage form, which consists essentially of tetrahydrolipstatin formulated as an oral composition, the amount of tetrahydrolipstatin being effective to alleviate or cure type II diabetes mellitus per se and in the range of from 60 to 720 mg of tetrahydrolipstatin per day, wherein the pharmaceutical preparation is to be administered from two to three times per day."

(ii) Auxiliary request 1:

"1. The use of tetrahydrolipstatin for the manufacture of an oral pharmaceutical preparation for treating type II diabetes mellitus, the amount of tetrahydrolipstatin to be employed in unit dosage form, which consists essentially of tetrahydrolipstatin formulated as an oral composition, the amount of tetrahydrolipstatin

being effective to alleviate or cure type II diabetes mellitus and in the range of from 60 to 720 mg of tetrahydrolip-statin per day, wherein the pharmaceutical preparation is to be administered from two to three times per day."

(iii) Auxiliary request 2:

"1. The use of tetrahydrolipstatin for the manufacture of an oral hypoglycemic pharmaceutical preparation for treating type II diabetes mellitus, the amount of tetrahydrolipstatin to be employed in unit dosage form, which consists essentially of tetrahydrolipstatin formulated as an oral composition, the amount of tetrahydrolipstatin being effective to alleviate or cure type II diabetes mellitus and in the range of from 60 to 720 mg of tetrahydrolipstatin per day, wherein the pharmaceutical preparation is to be administered from two to three times per day."

(iv) Auxiliary request 3:

"1. The use of tetrahydrolipstatin for the manufacture of an oral pharmaceutical preparation for treating type II diabetes mellitus in a non-obese subject, the amount of tetrahydrolipstatin to be employed in unit dosage form, which consists essentially of tetrahydro-lipstatin formulated as an oral composition, the amount of tetrahydrolipstatin being effective to alleviate or cure type II diabetes mellitus in a non-obese subject and in the range of from 60 to 720 mg of tetrahydrolip-statin per day, wherein the pharmaceutical preparation is to be administered from two to three times per day."

XIII. The appellant's arguments regarding the objections raised in connection with the allowability of the amendments and the requirements of Article 123(3) EPC can be summarised as follows:

The introduction of the feature "for treating type II diabetes mellitus per se", which had not been originally disclosed, changed the technical teaching of the contested patent. Now, the claimed use involved direct treatment of type II diabetes mellitus (NIDDM), i.e. treatment independent of weight loss, for which there was no basis in the original application. On the contrary: example 4 unambiguously showed that the glycemic control was not independent of weight loss. Moreover, there was no basis in the original application for the substitution of "consisting essentially of" for "comprising" either. According to the established jurisprudence of the boards of appeal, the term "consisting essentially of" excluded the presence of further compounds in addition to the active agent that might influence the properties of the oral pharmaceutical preparation defined in the claim. In view of the fact that excipients had a considerable influence on the performance of the preparation, neither examples 1 to 3 nor any other disclosure of the original application could serve as a basis for "consisting essentially of". Deletion of the term "per se" from claim 1 of auxiliary request I resulted in an extension of the scope of protection, which was not allowable under Article 123(3) EPC.

XIV. The respondent's arguments in connection with the allowability of the amendments and the requirements of Article 123(3) EPC can be summarised as follows:

Regarding the main request, the respondent emphasised that claim 1 concerned a second medical use claim. Second medical use claims were intention-based and linked to the treatment of a specific disease. The introduction of "per se" did not change the meaning of the claim at all but merely emphasised this aspect. In contrast to the prior art, which was directed to the use of tetrahydrolipstatin for treating obesity and hyperlipidemia, the present invention concerned, for the first time, direct treatment of NIDDM by means of glycemic control, which meant treatment independent of weight loss. This teaching was clearly expressed on pages 1 and 2 of the description, so that the specific examples were not needed as a basis for the amendments. Example 4, which did not relate to a formulation but concerned a clinical study involving patients stabilised with sulfonylureas, was irrelevant for interpreting the subject-matter defined in the claims.

In connection with the substitution of "consisting essentially of" for "comprising", reference was made to decision T 0468/99 of 16 May 2003, according to which "consisting essentially of" excluded the presence of further pharmaceutically active ingredients beside tetrahydroplistatin. This did not, however, exclude the presence of further compounds such as excipients. The original application as well as examples 1-3 provided a sufficient basis for the teaching that tetrahydro-lipstatin alone was able to achieve the desired pharmacological effect.

As the addition of "per se" did not change the technical teaching of the claimed use, its deletion

could not extend the scope of protection either. As a consequence, the subject-matter of auxiliary request I met the requirements of Article 123(3) EPC.

The filing of auxiliary requests II and III was the consequence of the board's reading of the term "per se", which could only be understood at the oral proceedings. As a consequence, it had not been possible to file these requests at an earlier stage of the appeal proceedings. The basis for claim 1 of auxiliary request II was page 1, lines 8-9 ("Other types of treatment include oral hypoglycemics and insulin"), in combination with the disclosure starting on page 1, line 23. The basis for claim 1 of auxiliary request III could be found on page 1, lines 7-8 ("The initial approach in treating obese patients affected with type II diabetes mellitus is weight reduction"), in combination with the disclosure starting on page 1, line 23.

XV. The appellant requested that the decision under appeal be set aside and the European patent No. 1 017 408 be revoked.

XVI. The respondent requested that the appeal be dismissed and the patent be maintained on the basis of the main request or, alternatively, of the first auxiliary request, both submitted with letter of 8 March 2012, or on the basis of the second or third auxiliary request received during oral proceedings of 13 March 2012.

Reasons for the Decision

1. The appeal is admissible.

2. Admission of the new requests

2.1 Main request and auxiliary request I

These requests had initially been filed as auxiliary requests II and III with letter dated 9 February 2012 and were resubmitted as main request and auxiliary request I with letter dated 5 March 2012. They constitute a reaction to objections raised in the board's communication pursuant to Article 15(1) RPBA of 17 November 2011. They are therefore admissible (Article 13(1) RPBA).

2.2 Auxiliary requests II and III

These requests were submitted at a late stage of the oral proceedings. In view of the fact that the amendments made were simple, straightforward and foreseeable and that they did not put the opponent and sole appellant into a worse position than if he had not appealed, the board admitted them into the proceedings (Article 13(1) RPBA).

3. Main request - amendments

3.1 Substitution of "consisting essentially of" for "comprising"

Claim 1 of the main request includes a unit dosage form, which consists essentially of tetrahydrolipstatin

formulated as an oral composition. Before evaluating whether the original application in its entirety specifically discloses such a unit dosage form, it first has to be established what the term "consisting essentially of", which cannot be found in the original application, means in this context.

The appellant, making reference to decision T 0468/99, argued that "consisting essentially of" meant that the claimed composition must not contain any additional components that might influence the properties of the composition, which even excluded excipients such as PVP or microcrystalline cellulose. The consequence of such an interpretation would be that the unit dosage form formulated as an oral composition would be restricted to tetrahydrolipstatin per se, as any additional compound would have some effect on the properties of the composition.

However, claims should be read in a technically reasonable way. Unit dosage forms formulated as oral compositions necessarily comprise a vehicle or carrier for the active agent, otherwise a safe administration of the active agent is not possible. This requires the presence of further compounds or excipients, which, as was mentioned above, have an influence on the properties of the composition in terms of release rate, stability etc. As a consequence, "consisting essentially of" cannot have this restrictive meaning in the present case. The board concludes that under the specific circumstances of the present case "consisting essentially of" excludes further active agents useful in the treatment of NIDDM but allows the presence of

additional compounds forming the carrier of tetrahydrolipstatin.

The passage on page 1, lines 23-27, of the original application discloses that tetrahydrolipstatin, when administered orally, is useful in the treatment and prevention of NIDDM. This disclosure does not specifically mention that tetrahydrolipstatin is used in the absence of further active agents. However, the passage on page 2, lines 22-23, indicates that the pharmaceutical preparations "**can also** contain still other therapeutically valuable substances" [emphasis by the board], which means that the absence of such therapeutically valuable substances is clearly envisaged. Furthermore, all three formulation examples (examples 1 to 3) concern compositions with tetrahydrolipstatin as the only active agent. The board concludes therefrom that treatment of NIDDM with oral compositions comprising tetrahydrolipstatin as the sole active agent constitutes the most preferred embodiment of the original application. As a consequence, the substitution of "consisting essentially of" for "comprising" is allowable under Article 123(2) EPC.

3.2 Addition of the feature "for treating type II diabetes mellitus per se"

This feature is not explicitly mentioned in the original application either. As a first step, it is necessary to construe the meaning of "for treating type II diabetes mellitus per se". The board agrees with the respondent that this expression defines a treatment which is independent of weight loss. As a next step, it has to be evaluated whether or not the original

application contains an implicit disclosure thereof. In this context, it is noted that obesity is a well-known risk factor for NIDDM and that weight loss is not merely an unspecific preventive activity but constitutes a concrete form of treatment of NIDDM (see the first sentence and in particular the second sentence of the summary of document (11), which indicates that reduction of weight excess comes to the front line in the prevention and **management** of NIDDM [emphasis by the board]). This is confirmed in the original application on page 1, lines 7-8, which read: "The initial approach in **treating** obese patients affected with type II diabetes mellitus is weight reduction" [emphasis by the board]. As a consequence, treatment of NIDDM which is independent of weight loss, and treatment of NIDDM by weight loss, represent two subcategories of the treatment of NIDDM in general.

The respondent argued that page 1 of the original application contained a specific disclosure of the use of tetrahydrolipstatin for the treatment of type II diabetes mellitus per se. In particular, reference was made to the fact that the passage in lines 18-21, which concerns a prior-art citation (US-A-4 598 089), according to which tetrahydrolipstatin is a known compound useful for the control or prevention of obesity and hyperlipidemia, was immediately followed by the statement "[i]t has now surprisingly been found that a gastrointestinal lipase inhibitor, preferably tetrahydrolipstatin, when administered orally, is useful in the treatment and prevention of type II diabetes mellitus", which, according to the respondent, could in this context only mean treatment and

prevention of type II diabetes mellitus per se, i.e. independent of weight loss.

The board cannot follow this reasoning: the passage on page 1, lines 18-27 says that in the prior art, tetrahydrolipstatin was used for the treatment of obesity and hyperlipidemia. In contrast, the present invention concerns the use of tetrahydrolipstatin for the treatment of type II diabetes mellitus, i.e. type II diabetes mellitus in general. There is, however, no reference in this passage as to whether said treatment is associated with or independent of weight loss. In other words, the subcategory "treatment of type II diabetes mellitus independent of weight loss" is not specifically disclosed therein.

This conclusion is not changed by the fact that the use of tetrahydrolipstatin for treating type II diabetes mellitus treatment is characterised as "surprising" (see page 1, line 23). It might be argued that including this judgmental term constitutes a pointer towards treatment of type II diabetes mellitus independent of weight loss, as treatment in combination with weight reduction would not be surprising in view of the statements further up on page 1 that (a) the initial approach in treating obese patients affected with type II diabetes mellitus is weight reduction (page 1, lines 7-8) and (b) tetrahydrolipstatin is known to be useful for the control or prevention of obesity and hyperlipidemia (page 1, lines 18-21). However, the disclosure of an amendment in the original application, no matter whether it is explicit or implicit, must be unambiguous and can therefore not be based on an evaluation of what the author of the

original application might or might not consider as surprising. Moreover, the skilled person will read the original application in its entirety and learn from example 4 that weight reduction is an important issue in the present invention. Example 4, which concerns a study of patients suffering from NIDDM, emphasises that 30% of patients treated with tetrahydrolipstatin achieved at least a 5% reduction in baseline body weight.

The board therefore comes to the conclusion that the original application does not specifically disclose, neither by explicit nor by implicit disclosure, the use of tetrahydrolipstatin for the manufacture of an oral pharmaceutical preparation for treating type II diabetes mellitus per se, i.e. independent of weight reduction. The requirements of Article 123(2) EPC are therefore not met.

4. Auxiliary request I - Article 123(3) EPC

Deletion of "per se" from claim 1 of auxiliary request I means that, in contrast to the claims as granted, treatment by tetrahydrolipstatin is no longer restricted to type II diabetes mellitus independent of weight reduction, but encompasses treatment of any type of type II diabetes mellitus. In other words, the scope of protection has been extended from the treatment of a specific subcategory of NIDDM to NIDDM in general. As a consequence, the requirements of Article 123(3) EPC are not met.

5. Auxiliary request II - Article 123(2) EPC

Compared to the main request, the subject-matter of claim 1 of auxiliary request II has been narrowed down to the use of tetrahydrolipstatin for the manufacture of an oral **hypoglycemic** pharmaceutical preparation for treating type II diabetes mellitus. Such a use is not mentioned in the original application. The passage on page 1, lines 7-9, indicates that the initial treatment of obese patients affected with NIDDM is weight reduction and that other types of treatment include oral hypoglycemics and insulin. However, the combination of this passage, which concerns the prior art, with the statement in lines 23-25 of the same page that it has now surprisingly been found that tetrahydrolipstatin, when administered orally, is useful in the treatment and prevention of type II diabetes mellitus, does not provide a basis for its use for the manufacture of an oral hypoglycemic pharmaceutical preparation as claimed in claim 1 of auxiliary request II. As was already mentioned above (see third paragraph of point 3.2), the original application discloses the use of tetrahydro-lipstatin for the treatment of NIDDM in general. There is, however, no basis for the specific subcategory (dependent or independent, hypoglycemic, etc.). As a consequence, the requirements of Article 123(2) EPC are not met.

6. Auxiliary request III - Article 123(2) EPC

6.1 Compared to the main request, the subject-matter of claim 1 of auxiliary request III additionally comprises a disclaimer disclaiming obese subjects, thus

restricting the treatment of NIDDM to non-obese subjects. According to decision G 2/10 of 30 August 2011, an amendment to a claim by the introduction of a disclaimer disclaiming from it subject-matter disclosed in the application as filed infringes Article 123(2) EPC if the subject-matter remaining in the claim after the introduction of the disclaimer is not, be it explicitly or implicitly, directly and unambiguously disclosed to the skilled person, using common general knowledge, in the application as filed (see point 1a of the order).

The original application discloses on page 1, lines 7-9 that the initial approach in treating obese patients affected with type II diabetes mellitus is weight reduction. Later on (see page 1, lines 18-21), tetrahydrolipstatin is mentioned as a known compound useful for the control or prevention of obesity and hyperlipidemia. However, as pointed out in point 5 above in connection with claim 1 of auxiliary request II, the combination of these passages concerning the prior art with the statement in lines 23-25 of the same page that it has now surprisingly been found that tetrahydrolipstatin, when administered orally, is useful in the treatment and prevention of type II diabetes mellitus, does not provide a basis for its use for the manufacture of an oral hypoglycemic pharmaceutical preparation for specific administration to non-obese patients. As mentioned above (see third paragraph of point 3.2), the original application discloses the use of tetrahydrolipstatin for the treatment of NIDDM in general. There is, however, no direct and unambiguous basis, be it by explicit or implicit disclosure, for specific subcategories such as

the treatment of NIDDM in non-obese subjects. As a consequence, the requirements of Article 123(2) EPC are not met.

7. Reimbursement of the appeal fee

According to Article 113(1) EPC, the decisions of the European Patent Office may only be based on grounds or evidence on which the parties concerned have had an opportunity to present their comments. Established jurisprudence has interpreted this provision to mean that the comments presented must be considered in the ensuing decision. Thus, a decision which fails to take explicitly into account potentially refutative arguments submitted by a party contravenes Article 113(1) EPC, thereby constituting a substantial procedural violation (see decision T 0246/08 of 14 August 2008, point 2.2 of the reasons for the decision). In the present case, the contested patent was opposed inter alia under Article 100(b) EPC for insufficiency of disclosure. This ground of opposition was discussed at the oral proceedings. However, the decision under appeal, in which the patent and the invention to which it relates were found to meet the requirements of the EPC, does not contain any reasoning at all in connection with insufficiency of disclosure. Therefore, a substantial procedural violation has occurred.

The minutes of the oral proceedings reveal (see first paragraph on page 2) that the chairman of the opposition division announced after deliberation that the requirements of Article 83 EPC were met and that Article 100(b) EPC did not prejudice the maintenance of

the patent, which means that the failure to consider sufficiency of disclosure had no influence on the final decision to maintain the patent in amended form. As a consequence, the board concludes that reimbursement of the appeal fee is not equitable, as the substantial procedural violation was not sufficiently closely linked to the need to pay the appeal fee.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

3. The request for reimbursement of the appeal fee is refused.

The Registrar: The Chairman:

N. Maslin U. Oswald