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Datasheet for the decision of 12 March 2008

Case Number: T 1652/06 - 3.3.02

Application Number: 98945529.0

Publication Number: 0979651

IPC: A61K 31/557

Language of the proceedings: EN

Title of invention:
Portal hypertension inhibitor

Applicant:
Sucampo AG

Headword:
Treatment of portal Hypertension/SUCAMPO AG

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

Relevant legal provisions (EPC 1973):
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Keyword:
"Main and first auxiliary requests- "Novelty (no): treatment of portal hypertension requires lowering of pressure in the portal vein"
"Second and third auxiliary requests - Article 123(2) (no): features taken from the background art cannot serve as basis for amendments"

Decisions cited:
G 0002/88

Catchword:
-

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Case Number: T 1652/06 **-** 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 12 March 2008

Appellant: Sucampo AG
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 26 May 2006 refusing European application No. 98945529.0 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: J. Riolo
Members: A. Lindner
P. Mühlens

Summary of Facts and Submissions

I. European patent application No. 98 945 529.0 (publication No. EP-A-0 979 651) was refused by a decision of the examining division dated 27 April 2006 on the basis of Article 97(1) EPC 1973 on the grounds of lack of novelty and non-compliance with the requirements of Article 123(2) EPC.

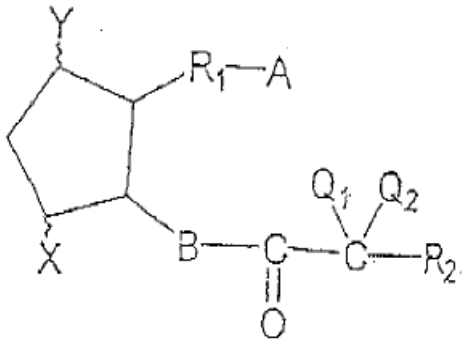
II. The following documents, cited during the proceedings before the examining division and the board of appeal, are relevant to the present decision:

(1) EP-A-0 690 049
(2) Gastroenterology Clinics of North America, 1992, vol. 21, no. 1, pages 15-40

III. The decision was based on claims 1-8 of the main and first to fourth auxiliary requests, all filed in a letter dated 27 March 2006.

Independent claim 1 of the main request before the examining division reads as follows:

"1. The use of a 15-keto-prostaglandin compound of formula (I) for the manufacture of a medicament for suppressing increased portal vein pressure, wherein formula (I) is:



wherein X and Y are hydrogen, hydroxy, halogen, straight or branched C_{1-6} alkyl, hydroxy straight or branched (C_{1-6}) alkyl, or oxo, with the proviso that at least one of X and Y is a group other than hydrogen, and the 5-membered ring may have at least one double bond;

A is $-CH_2OH$, $-COCH_2OH$, -COOH or a functional derivative thereof;

B is $-CH_2-CH_2-$, -CH=CH- or $-C\equiv C-$;

Q_1 and Q_2 are hydrogen, halogen or straight or branched C_{1-6} alkyl;

R_1 is a bivalent saturated or unsaturated, straight or branched chain hydrocarbyl group having 1 to 14 carbon atoms, which is unsubstituted or substituted with halogen, oxo or aryl;

R_2 is a saturated or unsaturated, straight or branched chain hydrocarbyl group having 1 to 14 carbon atoms which is unsubstituted or substituted with halogen, oxo, hydroxy, straight or branched C_{1-6} alkoxy, straight or branched C_{1-6} alkanoyloxy, cyclo C_{1-6} alkyl, aryl or aryloxy."

IV. The arguments in the decision may be summarised as follows:

The subject-matter of claim 1 of the main and first auxiliary requests was not novel because document (1) related to the treatment of portal hypertension, which automatically implied suppression of increased portal vein pressure. This fact was not changed by the disclosure in document (2), which referred to some "miscellaneous agents" such as metoclopramide as agents for the treatment of portal hypertension which did not lower the portal pressure, as the person skilled in the art would not consider them as portal hypotensive agents, but only as agents for the treatment of variceal haemorrhages.

Likewise, the subject-matter of claim 1 of the second auxiliary request was not novel over document (1), as the additional feature "directly affecting portal vein pressure" only defined the mechanism of action underlying the hypotensive effect.

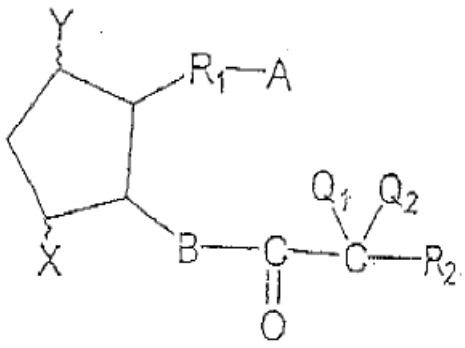
The subject-matter of claim 1 of the third auxiliary request was not allowable under Article 123(2) EPC, as the feature "hypertension due to occlusion or congestion of the portal venous system" was only disclosed in connection with the background art, but not as part of the present invention. Moreover, the "test example" could not serve as the basis for this feature, either, as it had been presented as supportive evidence for the treatment of portal hypertension in general.

Claim 1 of the fourth auxiliary request did not meet the requirements of Article 123(2) EPC on account of an unallowable disclaimer.

V. The appellant (applicant) lodged an appeal against the said decision.

VI. With the statement of the grounds of appeal dated 5 October 2006, the appellant filed new main, first auxiliary and second auxiliary requests. Claim 1 of the main request reads as follows:

"1. The use of a 15-keto-prostaglandin compound of formula (I) for the manufacture of a medicament for suppressing increased portal vein pressure, wherein formula (I) is:



wherein X and Y are hydrogen, hydroxy, halogen, straight or branched C_{1-6} alkyl, hydroxyl straight or branched (C_{1-6}) alkyl, or oxo, with the proviso that at least one of X and Y is a group other than hydrogen, and the 5-membered ring may have at least one double bond;
A is $-CH_2OH$, $-COCH_2OH$, -COOH or a functional derivative thereof;

B is $-CH_2-CH_2-$, $-CH=CH-$ or $-C\equiv C-$;
Q_1 and Q_2 are hydrogen, halogen or straight or branched C_{1-6} alkyl;
R_1 is a bivalent saturated or unsaturated, straight or branched chain hydrocarbyl group having 1 to 14 carbon atoms, which is unsubstituted or substituted with halogen, oxo or aryl;
R_2 is a saturated or unsaturated, straight or branched chain hydrocarbyl group having 1 to 14 carbon atoms which is unsubstituted or substituted with halogen, oxo, hydroxy, straight or branched C_{1-6} alkoxy, straight or branched C_{1-6} alkanoyloxy, cyclo C_{1-6} alkyl, aryl or aryloxy."

Claim 1 of the first auxiliary request reads as follows:

"1. The use of a 15-keto-prostaglandin compound of formula (I) for the manufacture of a portal hypotensive agent, wherein formula (I) is:" (see claim 1 of the main request).

Claim 1 of the second auxiliary request reads as follows:

"1. The use of a 15-keto-prostaglandin compound of formula (I) for the manufacture of a medicament for treating pre sinusoidal portal vein hypertension, wherein formula (I) is:" (see claim 1 of the main request).

VII. In the oral proceedings of 12 March 2008, the appellant filed a new third auxiliary request, of which claim 1 reads as follows:

"1. The use of a 15-keto-prostaglandin compound of formula (I) for the manufacture of a medicament for treating portal hypertension due to occlusion or congestion of the portal venous system, wherein formula (I) is:" (see claim 1 of the main request).

VIII. The appellant's submissions, both in the written procedure and at the oral proceedings, can essentially be summarised as follows:

In connection with the main and first auxiliary requests, it was held that document (1) disclosed the use of prostaglandins encompassed by formula (I) of the present application for the treatment of hepato-biliary diseases and of conditions having an etiology based on hepato-biliary diseases. Portal hypertension was one example in a long list of disorders linked to hepato-biliary diseases. Document (1) did not disclose direct treatment of portal hypertension, nor was there any indication that treatment of portal hypertension would suppress increased portal vein pressure. The fact that treatment of portal hypertension did not have to involve suppression of portal vein pressure was clearly shown in document (2), where active agents such as metoclopramide were used without lowering the portal vein pressure.

As regards the subject-matter of claim 1 of the second auxiliary request, it was held that although the basis for the feature "for treating pre sinusoidal portal vein hypertension" was taken from a passage referring to the background art, the information disclosed therein was nevertheless part of the present invention and could therefore be used as the basis for the

amendments made, particularly as the test example was a model for pre sinusoidal portal hypertension.

The same reasoning was applied to the subject-matter of claim 1 of the third auxiliary request, where the feature "for treating occlusion or congestion of the portal venous system" was also based on a passage relating to the background art.

IX. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of one of the main, first or second auxiliary requests filed with the grounds of appeal, or on the basis of the third auxiliary request filed in the oral proceedings.

Reasons for the decision

1. The appeal is admissible.

2. Admissibility of the third auxiliary request filed during the oral proceedings of 12 March 2008:

Compared with the previous third auxiliary request dealt with in the decision under appeal, the amendments made involve only minor linguistic changes. The new third auxiliary request is therefore admissible.

3. Main request - novelty:

3.1. Document (1) discloses the use of 15-keto-prostaglandins corresponding to formula (I) of the present application for treating hepato-biliary

diseases (see page 3, lines 1-23). According to page 3, lines 29-35, the term "hepato-biliary disease" includes "all conditions having etiology based on or accompanied by disorder of hepatocyte ... or ... of biliary tract", of which portal hypertension is one example specifically mentioned in a list of about 25 diseases. Document (1) does not explicitly disclose the feature "for suppressing increased portal vein pressure" as now claimed. As a consequence, it has to be established, whether this feature is implicitly disclosed in document (1).

3.2. Portal hypertension is an increase in blood pressure in the portal vein. As a consequence, it appears that its treatment, which is disclosed in document (1), inevitably requires suppression of the increased blood pressure in the affected area, i.e. in the portal vein.

Decision G 2/88 (OJ EPO 1990, 93) stipulates that the recognition or discovery of a previously unknown property of a known compound, such property providing a new technical effect, can clearly involve a valuable and inventive contribution to the art (Reasons 2.3).

In the present case, however, the subject-matter as claimed and the disclosure in document (1) rely on the same technical effect. The feature "for suppressing increased portal vein pressure" does not provide any new technical information to the skilled reader with regard to document (1). As a consequence, the subject-matter of claim 1 of the main request is not novel (Article 54 EPC).

3.3. Arguments submitted by the appellant:

3.3.1. In order to demonstrate that the treatment of portal hypertension does not necessarily have to cause a reduction of the portal vein pressure, the appellant submitted document (2). This document lists three groups of active agents which can be used in the treatment of portal hypertension, namely vasoconstrictors and vasodilators, which reduce portal pressure, and a miscellaneous group of drugs including metoclopramide, domperidone and pentagastrin, which reduce the blood flow and pressure in the gastroesophagal variceal system without, however, lowering the portal pressure (see page 17, first complete paragraph and page 18, Table 1). From this, the conclusion might be drawn that "treatment of portal hypertension" is more generic than "suppression of increased portal vein pressure". In that case, the latter feature would not be specifically disclosed in document (1) by means of implicit disclosure, as a selection could be made between treatment of portal hypertension with or without reduction of the portal vein pressure.

It is correct that the agents belonging to the miscellaneous group in document (2) do not lower the portal blood pressure. However, when it comes to deciding whether these agents are or are not portal hypotensive agents, the general teaching of document (2) has to be taken into account, which is reflected in the paragraph bridging pages 16 and 17 and reads as follows:

> "The pharmacologic therapy of portal hypertension is aimed at the treatment of an acute variceal bleed and the prevention

> of hemorrhage or rebleeding. The agents used during a variceal hemorrhage should decrease the portal pressure (ΔTP) and the size of the tear. Those agents used in the chronic treatment of portal hypertension should aim at reducing the portal pressure and the factors leading to an increase in the variceal wall tension."

From this citation the skilled person concludes that the treatment of portal hypertension has to include a reduction of the portal pressure. The examining division therefore argued correctly in the decision under appeal that the agents in the miscellaneous group in document (2) were not portal hypotensive agents for treating portal hypertension, but only agents for the treatment of variceal hemorrhages. As a consequence, document (2) does not provide any evidence that treatment of portal hypertension is more generic than lowering the pressure in the affected area, i.e. in the portal vein.

In addition, the agents belonging to the miscellaneous group are structurally remote from the compounds according to formula (I) of the application under appeal.

3.3.2. Document (1) is concerned with the treatment of hepato-biliary diseases rather than with the direct treatment of portal hypertension:

The expression "direct treatment of portal hypertension" appears to mean that the drug acts directly at the site of the portal hypertension, i.e. the portal vein, instead of indirectly lowering the portal pressure by treating hepato-biliary diseases. In this context, the board wants to point out that the

subject-matter of the present claim 1 is not limited to the direct treatment of portal hypertension but comprises all types including those which are related to or caused by hepato-biliary diseases.

3.4. As a consequence, the arguments submitted by the appellant cannot succeed.

4. First auxiliary request - novelty:

The reasoning as outlined above for the main request fully applies to claim 1 of the first auxiliary request: the compounds of document (1) which are used for the treatment of portal hypertension and which indeed lower increased portal vein pressure are inevitably portal hypotensive agents. As a consequence, the subject-matter of claim 1 of the first auxiliary request is not novel (Article 54 EPC).

5. Second auxiliary request - amendments:

5.1. The feature "for treating pre sinusoidal portal hypertension" is taken from page 1, line 16 of the application as originally filed, where the factors contributing to the etiology of portal hypertension are classified into pre sinusoidal and post sinusoidal conditions. This passage, however, merely reflects the background art, which is not related to the teaching of the present invention. There is no specific disclosure in the application as originally filed that the 15-keto-prostaglandins according to formula (I) are applicable for the treatment of pre sinusoidal portal vein hypertension. On page 4, lines 12-15, it is mentioned that it was an object of the invention to

"provide an anti-portal hypertensive agent useful for treatment to suppress increased portal vein pressure that occurs due to **various factors**" [emphasis by the board]. However, these various factors cannot be interpreted in the light of the background art as cited in the introductory part of the application under appeal.

5.2. The board disagrees with the appellant's argument that it would not make any difference whether the feature "for treating pre sinusoidal portal hypertension" was disclosed in connection with the background art or on page 4 in the section "summary of the invention": if it were disclosed in the section "summary of the invention", it would be part of the present invention and could therefore in principle be included in claim 1. As it was disclosed in connection with the background art, however, it cannot be considered as part of the present invention.

5.3. The appellant also cited the test example, where the portal vein of a rat was obstructed, as a model for pre sinusoidal portal hypertension. In the test example, however, a single compound (13,14-dihydro-15-keto-16,16-difluoro-18S-methyl-prostaglandin E1) was used. Starting from the test example, a two-fold generalisation has to be made in order to arrive at the subject-matter of the present claim 1: firstly, a specific active agent has to be generalised to any compound corresponding to formula (I) and secondly, in terms of the disease to be treated, obstruction of the portal vein has to be generalised to any type of pre sinusoidal portal vein hypertension. As a consequence, the test example cannot serve as the basis for the

feature "for treating pre sinusoidal portal vein hypertension" either.

5.4. It follows from this that the subject-matter of claim 1 of the second auxiliary request includes a combination of features (selection of active agent according to formula (I) + treatment of pre sinusoidal portal vein hypertension) that has no basis in the application as originally filed. The requirements of Article 123(2) EPC are therefore not met.

6. Third auxiliary request - amendments:

6.1. The reasoning of point 5 above in connection with the second auxiliary request applies ***mutatis mutandis*** to the subject-matter of the third auxiliary request: in the application as originally filed, the feature "for treating portal hypertension due to occlusion or congestion of the portal venous system" is only disclosed as part of the background art (see page 1, lines 13-16). Again there is no general teaching that the 15-keto-prostaglandins according to formula (I) are applicable for the treatment of the specific type of portal hypertension as now claimed. Again a distinction has to be made as to whether in the application as originally filed the feature in question is disclosed as part of the background art or as part of the invention (see point 5.2 above).

6.2. As regards the test example, again two generalisations are made. With regard to the active agent, see point 5.3 above. As far as the disease to be treated is concerned, obstruction of the portal vein was

generalised to any type of occlusion or congestion of the portal venous system.

6.3. As a consequence, the subject-matter of claim 1 of the third auxiliary request does not meet the requirements of Article 123(2) EPC either.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman

N. Maslin J. Riolo