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Case Number: T 0759/13 - 3.3.07

Application Number: 01921346.1

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Title of invention:
THE USE OF ANTICOAGULANT AGENTS IN THE EXTRACORPOREAL TREATMENT OF BLOOD

Applicant:
AbbVie Deutschland GmbH & Co KG

Relevant legal provisions:
EPC Art. 54(2), 54(5)

Keyword:
Novelty - novelty of use - second (or further) medical use (no)

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Case Number: T 0759/13 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 1 March 2016

Appellant: (Applicant)	AbbVie Deutschland GmbH & Co KG Max-Planck-Ring 2a 65205 Wiesbaden (DE)
Representative:	Reitstötter Kinzebach Patentanwälte Sternwartstrasse 4 81679 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 9 October 2012 refusing European patent application No. 01921346.1 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	J. Riolo
Members:	D. Semino
	D. T. Keeling

Summary of Facts and Submissions

I. The appeal lies from the decision of the Examining Division announced at oral proceedings on 13 September 2012 refusing European patent application No. 01 921 346.1.

II. The decision was based on a single set of claims filed with letter of 6 November 2011.

Claim 1 of that request read as follows:

"1. PEG (polyethylene glycol)-hirudin for use in the treatment of a subject suffering from chronic renal insufficiency, the subject requiring intermittent hemodialysis comprising extracorporeal circulation of blood, for effective anticoagulant protection during the extracorporeal circulation and for prophylaxis of vascular complications after the extracorporeal circulation."

III. According to the decision under appeal claim 1 lacked novelty over document D1 (WO-A-91/08229), which described the use of PEG-hirudin as anticoagulant in the treatment of extra-corporeal blood circulation in haemodialysis. Support for a high incidence of vascular complications in patients with chronic kidney disease and a high mortality rate could not be found, so that this issue was found not to be relevant for novelty. No difference related to the amount of PEG-hirudin to be administered could be acknowledged and the choice of the group of patients (those suffering from chronic renal failure) seemed arbitrary and did not lead to novelty. An effect of PEG-hirudin exerted after the extracorporeal circulation did not confer novelty to the claim, as both the application and D1 showed that

the blood concentration of PEG-hirudin remained stable long after injection, so that the level of disclosure of the application did not go beyond that of D1. The data in example 12 of D1 did not relate to patients suffering from chronic renal failure, but were indicative also for them.

IV. The applicant (appellant) lodged an appeal against that decision. With the statement setting out the grounds of appeal filed with letter of 19 February 2013, the appellant submitted four sets of claims as main request and auxiliary requests 1 to 3.

Claim 1 of the main request was identical to claim 1 of the request on which the decision was based. In claim 1 of auxiliary request 1 the "extracorporeal circulation of blood" was replaced by "repeating cycles of an extracorporeal phase wherein blood of said subject is circulated extracorporeally, and an intracorporeal phase wherein no blood of said subject is circulated extracorporeally, with a frequency of at least one extracorporeal circulation per week", the prophylaxis related to "a vascular complications" (in the singular) and it was specified that "the PEG-hirudin is adapted for being administered in form of a single dose per cycle at the start of the hemodialysis and the amount of the single dose administered for a cycle is adapted such that, at the end of the intracorporeal phase, a PEG-hirudin blood level having at least a value of 150 ng/ml is obtained". Claim 1 of auxiliary request 2 corresponded to claim 1 of auxiliary request 1 with the replacement of the "vascular complication" by "the formation of thrombi in the vascular system of the individual". Claim 1 of auxiliary request 3 corresponded to claim 1 of auxiliary request 1 with the specification that "the vascular complication is

selected from the group consisting of venous and arterial thromboses, peripheral occlusive diseases, shunt thromboses, catheter thromboses, thromboembolism, myocardial infarct, unstable angina pectoris and stroke".

V. In a communication sent in preparation of oral proceedings, the Board analysed the issues of sufficiency of disclosure and novelty and noted in this context *inter alia* that "it appears that the level of disclosure in the application does not go beyond what is disclosed in D1" (point 1.5, first sentence).

VI. Oral proceedings took place on 1 March 2016 in the absence of the appellant as announced with a letter of 25 February 2016.

VII. The appellant's arguments as present in the statement of grounds can be summarised as follows:

The examining division did not properly evaluate the two interrelated effects of PEG-hirudin, namely the anticoagulant protection during the extracorporeal circulation of blood and the prophylaxis of vascular complications after the extracorporeal circulation. While D1 disclosed the former, it did not disclose the two effects together and did not deal with patients suffering from chronic renal insufficiency and their high risk of vascular complications. The measurement of the blood concentration did not equate with providing protection in specific patients and the data on healthy dogs did not have any relevance for patients suffering from chronic renal failure. In addition D1 did not teach an amount effective for achieving the desired prophylactic effect. On that basis novelty should be acknowledged for claim 1 of the main request. As to the

auxiliary requests, the skilled person could not have expected that the indicated dosage could provide effective anticoagulant protection.

The appellant did not react to the communication of the Board.

VIII. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request or of one of auxiliary requests 1 to 3, all filed with letter of 19 February 2013.

Reasons for the Decision

Main request - novelty

1. The appellant accepted that document D1 discloses PEG-hirudin and its effect in anticoagulant protection during the extracorporeal circulation of blood in hemodialysis (see D1: claim 1; examples 9 and 10; paragraph bridging pages 6 and 7). The central question therefore is whether the specification of a further medical use ("and for prophylaxis of vascular complications after the extracorporeal circulation") and of a specific group of subjects ("a subject suffering from chronic renal insufficiency") renders claim 1 novel by virtue of the exception in Article 54(5) EPC.

1.1 In the application it is reported that a disproportionately high incidence of vascular complications is present in patients with chronic kidney disease, which leads to a high mortality rate (page 2, lines 21 to 36 of the application as filed). However, no specific source is indicated to support the

statement (there is only a general reference to "an increasing frequency of reports"), nor was any study carried out by the appellant for this purpose.

1.2 In addition, it is claimed that the administration of PEG-hirudin can provide prophylaxis of vascular complications after the extracorporeal circulation (see page 3, lines 6 to 17 of the application as filed and claim 1 of the main request). However, no data are available to show that by administration of PEG-hirudin a prophylactic effect is achieved, i.e. the incidence of vascular complications is reduced. In this respect, the only available data show that the blood levels of PEG-hirudin (and values of other parameters related to it) are maintained relatively stable in dialysis patients between dialysis cycles (example, tables and figures).

1.3 Even if the application neither shows that the problem of high incidence of vascular complications in patients suffering from chronic renal insufficiency exists, nor that it is solved (see points 1.1 and 1.2), the Board will assume to the advantage of the appellant that the problem of high incidence of vascular complications was indeed existent and known (i.e. that the mentioned reports actually existed) and that maintenance of stable blood levels of PEG-hirudin is understood by the skilled person at the time of filing of the application as a sufficient guarantee for the prophylaxis of vascular complications. While it is noted that if it were not the case, the application would lack sufficiency (Article 83 EPC), the consequence of these considerations is that, as the same level of knowledge is to be attributed to the skilled person reading the prior art, this person is therefore aware of the vascular complications and of the possibility of

avoiding them by maintaining the blood level of the anticoagulant after hemodialysis.

1.4 Document D1 not only discloses the use of PEG-hirudin for anticoagulant protection during the extracorporeal circulation of blood in hemodialysis, but also specifies that this kind of hirudin derivative shows a biological activity which is considerably extended in time (page 6, lines 28-31), which makes it superior for therapy and prophylaxis of thromboembolic diseases (page 6, lines 33-36). On top of that it is shown in D1 that the activity of PEG-hirudin (and therefore its blood level) is maintained over a time span of 80 hours in dogs to which it has been administered (example 12 and figures). While it is true that the data do not refer to human patients, but to healthy dogs, the teaching in the general part of D1 (paragraph bridging pages 6 and 7) together with this example makes it clear that PEG-hirudin remains at high blood level for a long period of time after it has been administered.

1.5 This disclosure together with the knowledge of the skilled person relative to the vascular complications and their prophylaxis through maintenance of the blood level of the anticoagulant (see point 1.3, above) renders the technical teaching in D1 the same as the technical teaching in the application. In other words, as expressed in several ways in the decision under appeal, it appears that the level of disclosure in the application does not go beyond what is disclosed in D1.

1.6 With regard to the group of patients, subjects suffering from chronic renal insufficiency are not distinguished from those requiring hemodialysis by extracorporeal circulation (as disclosed in D1, page 6, line 38), so that also the subjects to be treated

cannot constitute a distinguishing feature with respect to the disclosure in D1.

1.7 As to the amount of the medicament, it is noted that claim 1 of the main request does not specify any amount and, as no tests are available to show which amount should be necessary to accomplish the desired prophylaxis, it can only be assumed that a usual amount of anticoagulant is administered, which does not constitute a difference with respect to the disclosure in D1 (a typical dosage is disclosed on page 7, lines 13-16).

1.8 On that basis the second medical use of claim 1 of the main request is not novel over the disclosure in document D1.

Auxiliary request 1 - novelty

2. In auxiliary request 1 a number of amendments are introduced, all of which relate to the formulation of the second medical use for the known medicament. The question is therefore to be answered whether any of these amendments is able to identify a new medical treatment, which constitutes a difference with respect to the disclosure of document D1.

2.1 The replacement of "extracorporeal circulation of blood" with "repeating cycles of an extracorporeal phase wherein blood of said subject is circulated extracorporeally, and an intracorporeal phase wherein no blood of said subject is circulated extracorporeally, with a frequency of at least one extracorporeal circulation per week" amounts only to a more detailed explanation of what is normally meant by hemodialysis treatment of patients suffering from

chronic renal insufficiency and does not change the scope of the claim. Similarly, the amendment of "vascular complications" to "a vascular complication" with regard to the prophylaxis does not have any impact on the analysis of novelty.

2.2 With regard to the indication of a dosage, it is noted that the wording adopted ("the PEG-hirudin is adapted for being administered in form of a single dose per cycle at the start of the hemodialysis and the amount of the single dose administered for a cycle is adapted such that, at the end of the intracorporeal phase, a PEG-hirudin blood level having at least a value of 150 ng/ml is obtained") does not specify a quantity to be administered, but defines the dosage by means of a result to be achieved, for which no information is present in the application as to whether this should correspond to an unusual amount of medicament, nor whether any specific result (in terms of treatment or prophylaxis) is achieved by such an administration. Under such circumstances and in the absence of proof of the contrary, it must be still assumed as for the main request that a usual amount of anticoagulant is administered, which does not constitute a difference with respect to the disclosure in D1 (a typical dosage is disclosed on page 7, lines 13-16).

2.3 On that basis it is concluded that claim 1 according to auxiliary request 1 lacks novelty over document D1.

Auxiliary requests 2 and 3 - novelty

3. Also the further amendments in claim 1 of auxiliary requests 2 and 3 relate to the formulation of the second medical use for the known medicament, so that the same question arises as for auxiliary request 1

(point 2, above). These further amendments specify that the vascular complication is "the formation of thrombi in the vascular system of the individual" (auxiliary request 2) or "is selected from the group consisting of venous and arterial thromboses, peripheral occlusive diseases, shunt thromboses, catheter thromboses, thromboembolism, myocardial infarct, unstable angina pectoris and stroke" (auxiliary request 3).

3.1 As far as these amendments are concerned, the same holds as detailed for the main request. Indeed also in this case no evidence is present that these complications are present, nor that they are reduced by means of the medicament, so that it can only be assumed that the skilled person is aware of the specific complications and knows that by maintaining the medicament blood level over time one achieves an appropriate prophylaxis. With this knowledge the reading of document D1 results in the same teaching as according to claim 1 of auxiliary requests 2 and 3. On top of that D1 explicitly mentions therapy and prophylaxis of thromboembolic diseases (page 6, lines 33-36).

3.2 On that basis it is concluded that also claim 1 according to auxiliary requests 2 and 3 lacks novelty over document D1.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

S. Fabiani J. Riolo

Decision electronically authenticated