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D E C I S I O N
of 14 March 2006

Case Number: T 1138/04 - 3.3.02
Application Number: 98935752.0
Publication Number: 0998292
IPC: A61K 31/66
Language of the proceedings: EN

Title of invention:
Method for inhibiting bone resorption

Patent proprietor:
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Opponents:
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Richter Gedeon R.T.
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Headword:
Inhibit bone resorption/Merck

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
"Main and first to ninth auxiliary request - added matter -
yes: unallowable combination of parts of the application as
filed"

Decisions cited:

-

Catchword:

-



Case Number: T 1138/04 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 14 March 2006

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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 19 August 2004
revoking European patent No. 0998292 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
J. P. Seitz

Summary of facts and submissions

- I. European patent No. 0 998 292 based on application No. 98 935 752.0 and filed as international patent application No. PCT/US98/14796 was granted with 22 claims.

Claim 1 as granted read as follows:

"Use of alendronic acid or a pharmaceutically acceptable salt thereof, or a mixture thereof, for the manufacture of a medicament for inhibiting bone resorption in a human wherein said medicament is adapted for oral administration, in a unit dosage form which comprises from about 8.75 mg to 140 mg of alendronic acid or a pharmaceutically acceptable salt thereof, on an alendronic acid active weight basis, according to a continuous schedule having a periodicity from about once every 3 days to about once every 16 days."

- II. Opposition was filed against the granted patent under Article 100(a) EPC for lack of novelty and inventive step, under Article 100(b) EPC for insufficiency of disclosure and under Article 100(c) EPC for the subject-matter of the patent extending the content of the patent application as filed.

The following document was cited *inter alia* during the proceedings before the opposition division and the board of appeal:

(14) "Update: Bisphosphonate", LUNAR NEWS, LUNAR Corporation, Madison, WI 53713, July 1996, pages 23 to 24.

III. By its decision pronounced at oral proceedings on 20 July 2004 and posted on 19 August 2004, the opposition division revoked the patent under Article 102(1) EPC because neither the set of claims of the main request nor the sets of claims of the first, second and third auxiliary requests filed in writing and during the oral proceedings met the requirements of the EPC.

The subject-matter of the main request was not new with respect to various documents and did not meet the requirements of industrial applicability because of the feature of the administration schedule.

With respect to the set of claims of the first auxiliary request, the opposition division noted that it contained features that did not fulfil the requirements of Article 123(2) EPC when introduced to claim 1 in the context of a prevention of osteoporosis.

The subject-matter of the second and third auxiliary requests was regarded as not inventive over the teaching of document (14).

The opposition division stated that with respect to document (14) no technical effect related to the distinguishing features

- dosage of about 70 mg versus 80 mg and
- a preparation taking the form of a tablet or capsule versus oral administration

was apparent. Said features were to be considered as an arbitrary non-functional modification of the medical use known already from document (14). The claimed invention did not solve any technical problem over (14).

IV. The appellant (patent proprietor) lodged an appeal against said decision and requested that the patent be maintained on the basis of one of four requests submitted in its grounds of appeal.

V. With a letter dated 12 January 2006, the appellant replaced the set of claims of the main request and additionally submitted a fourth auxiliary request.

The subject-matter of claim 1 of the new main request reads as follows (Bold letters characterise the relevant differences with respect to claim 1 as granted):

"Use of alendronic acid or a pharmaceutically acceptable salt thereof, or a mixture thereof, for the manufacture of a medicament for inhibiting bone resorption **to treat osteoporosis** in a human **in need thereof**, wherein said medicament is adapted for oral administration, in a unit dosage form which comprises **about 70mg** of alendronic acid or a pharmaceutically acceptable salt thereof, on an alendronic acid active weight basis, according to a continuous schedule **having a once-weekly dosing interval, wherein said medicament is in the form of a tablet or a capsule.**"

The only difference in corresponding claim 1 of the first auxiliary request with respect to claim 1 of the main request is that the wording "or a capsule" was removed at its end.

The subject-matter of claim 1 of the second auxiliary request is directed to the

"Use of a pharmaceutically acceptable salt of alendronic acid for the manufacture ..."

with the rest of the wording of claim 1 being unchanged with respect to the wording of claim 1 of the first auxiliary request.

In the same way, claim 1 of the third auxiliary request is directed to the

"Use of the monosodium salt of alendronic acid for the manufacture ..."

and claim 1 of the fourth auxiliary request to the

"Use of the monosodium trihydrate salt of alendronic acid for the manufacture ...".

VI. On 14 March 2006, oral proceedings took place before the board in the presence of representatives of the appellant and representatives of the respondents (opponents 01 to 07).

During these oral proceedings the appellant introduced five further auxiliary requests. The wording of claim 1

of the fifth to ninth auxiliary request corresponds to the wording of claim 1 of the already cited main request and first to fourth auxiliary request with the sole amendment that in each of them the passage

"for inhibiting bone resorption to treat osteoporosis in a human in need thereof"

is substituted by the passage

"for inhibiting **abnormal** bone resorption **in an osteoporotic human**" (substantially changed words put in bold by the board).

VII. With respect to the admissibility of its requests, the appellant mainly argued that all claims on file had been reworded in order to overcome the objections raised in writing or during the oral proceedings.

It pointed out that the skilled person, in view of all the amendments made in the sets of claims of the different requests, would recognise no difference between the teaching of the current requests and the patent application as filed, and thus the amendments were correct with respect to Article 123(2) EPC.

The source of all features of the current claims in the claims and in the description as originally filed was indicated by the appellant. Additionally the passages linking these features in the appellant's opinion - as far as the features were to be found in a different context in the patent application as filed - were presented.

VIII. The respondents' arguments submitted in writing and during the oral proceedings may be summarised as follows:

In their view, the features introduced by the amendments added subject-matter that was not disclosed in the patent application as filed and, therefore, claim 1 of each of the requests respectively contravened Article 123(2) EPC.

Additionally, the question of clarity (Article 84 EPC) was addressed by the respondents because of the claimed subject-matter referring to a unit dose of "about 70mg" whilst from the description of the patent in suit it must be taken into account that "a precise pharmaceutically effective amount cannot be specified in advance".

Moreover, the requested subject-matter was at least obvious with respect to document (14) and the respondents emphasised that all advantages of the claimed subject-matter alleged by the appellant referred to a dosing of 10 mg per day and not to the closest state of the art represented by document (14).

IX. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of either his main request filed with letter dated 12 January 2006, or alternatively on one of his nine auxiliary requests respectively filed:

- first, second, third auxiliary requests with letter dated 21 December 2004,

- fourth auxiliary request with letter dated 12 January 2006,
- fifth to ninth auxiliary requests during the oral proceedings.

The respondents (opponents) requested that the appeal be dismissed.

Reasons for the decision

1. The appeal is admissible.
2. All the auxiliary requests represent a response to the arguments set out during the proceedings. They have to be regarded as an attempt to overcome the problems discussed and they are therefore admitted into the proceedings.
3. *Main request and first to fourth auxiliary requests; Article 123(2) EPC*
- 3.1 Claim 1 of all these requests is drafted in the format of a second medical use claim:

"The use of a substance or composition for the manufacture of a medicament for a specified new and inventive therapeutic application."

The therapeutic application for which in the present case the medicament has to be manufactured is defined by the wording

"- for inhibiting bone resorption

- to treat osteoporosis in a human in need thereof".

3.2 This wording consists of two therapeutic applications in combination:

- inhibiting bone resorption and
- treating osteoporosis

3.3 The patent application as filed refers to five independent therapeutic applications:

- inhibiting bone resorption (independent original claims 1 to 5, 28 to 29 and 32 to 33)
- treating osteoporosis (independent original claims 6 to 11)
- preventing osteoporosis (independent original claims 12 to 17)
- treating abnormal bone resorption (independent original claims 18 to 22)
- preventing abnormal bone resorption (independent original claims 23 to 27)

In the description, the therapeutic applications are distinguished by using the wording "another object" or "other embodiments" (see page 6, lines 15 to 24, together with page 7, lines 12 to 14, or page 7, line 20, to page 8, line 22, or page 12, lines 23 to 28) and different definitions are given to some of them (see page 11, lines 18 to 29).

Even the examples are directed to either treatment or prevention of osteoporosis (examples 2 to 5), to "treating or preventing osteoporosis or other conditions associated with abnormal bone resorption"

(example 6) or to "inhibiting bone resorption" (examples 7 and 8).

Thus, throughout the patent application as filed "inhibiting bone resorption" is separated from "treating of osteoporosis", that means no clear and unambiguous connection between them is recognisable.

Nevertheless, in claim 1 of the main request and of the first to fourth auxiliary requests the combination of these two therapeutic applications has been used to define the therapeutic application for which the medicament has to be manufactured.

3.4 There is no explicit definition of the meaning of this combination of two single therapeutic applications in the patent application as filed.

3.5 There are some statements in the patent application as filed where these two therapeutic applications are mentioned and the skilled person might at first glance have the impression of identifying some relationship between them:

(a) On page 14, lines 25 to 34, the appellant in its application discloses that

the methods and the compositions of the present invention were useful for

- inhibiting bone resorption and
- for treating abnormal bone resorption and
- for preventing abnormal bone resorption and
- conditions associated therewith.

Such a condition was both generalised and localised bone loss.

Generalised bone loss was often associated with osteoporosis.

From this passage in the patent application as filed it has to be inferred that its methods are also meant to be useful for the treatment of the condition known as osteoporosis with which generalised bone loss is often associated.

But it cannot be inferred whether they are useful for the treatment of osteoporosis because of their bone resorption inhibiting effect.

The reason is that osteoporosis is only associated with

- generalised bone loss,
whereas generalised bone loss itself is part of a condition associated with one of three different therapeutic applications, namely

- abnormal bone resorption to be treated or
- abnormal bone resorption to be prevented or
with
- bone resorption to be inhibited.

- (b) Via the "bone loss" part of the term "generalised bone loss" some relationship between osteoporosis and the therapeutic application "*bone resorption inhibiting*" may also be found in the definition of the wording "*bone resorption inhibiting*" on page 11, lines 23 to 29, of the patent application as filed:

"The term "bone resorption inhibiting", as used herein, means treating or preventing bone resorption by the direct or indirect alteration of osteoclast formation or activity. Inhibition of bone resorption refers to treatment or prevention of bone loss, especially the inhibition of removal of existing bone either from the mineral phase and/or the organic matrix phase, through direct or indirect alteration of osteoclast formation or activity."

But the association with osteoporosis is only mentioned together with generalised bone loss (ibid., page 14, line 34) whereas "localised bone loss" is mentioned as well (ibid., page 14, lines 32 to 33) and again there is no clear connection between these therapeutic applications that would allow the conclusion that they could be mentioned in combination.

- (c) Additionally, from other explanations in the patent application as filed, the appellant points out a relationship between "osteoporosis" and "abnormal bone resorption to be treated" (see page 1, lines 23 to 25, page 7, lines 12 to 14). But the treatment of "abnormal bone resorption" includes therapeutic applications other than "osteoporosis" (see e.g. page 1, lines 23 to 25).

3.6 Taking into account these existing explanations and definitions of the applicant, it must be concluded that the combination of the terms "inhibiting bone resorption" and "to treat osteoporosis" used in claim 1 of the main request and each of the first to fourth

auxiliary requests is neither disclosed literally nor by any explanation or definition throughout the patent application as filed. Consequently, the wording used as a combination of terms contains different subject-matter and means different therapeutic applications, insofar as the terms are regarded separately and even more specifically insofar as they are regarded in combination:

Thus, whichever term is used as starting point for finding in the patent application as filed the original disclosure of all the features incorporated in these claims 1,

either the "treatment of osteoporosis" or "inhibiting bone resorption",

once the second term is added, the therapeutic application has broadened and the combination refers to subject-matter extending the content of the patent application as filed.

4. *Fifth to ninth auxiliary requests; Article 123(2) EPC*

- 4.1 In claim 1 of all these cited requests, the therapeutic application for which the medicament has to be manufactured is defined by the wording "for inhibiting **abnormal** bone resorption **in an osteoporotic human**" (emphasis added by the board). This definition replaces the wording "for inhibiting bone resorption to treat osteoporosis in a human in need thereof" contained in the requests discussed above.

4.2 There is no explicit mention or definition of this wording in its amended form in the patent application as filed either.

Only the terms "treatment of abnormal bone resorption", "prevention of abnormal bone resorption" and a definition of "abnormal bone resorption" can be found.

4.2.1 The citations "treatment ..." or "prevention of abnormal bone resorption" do not refer to "inhibiting":

On page 7, lines 12 to 14, it is mentioned that it was "another object of the present invention to treat or prevent abnormal bone resorption in an osteoporotic mammal, preferably an osteoporotic human", with no reference to the text either before or after these lines.

On page 8, lines 16 to 22, it is only mentioned that from about 8.75 mg to about 140 mg of a bisphosphonate may be administered to a human either to inhibit bone resorption or to treat or to prevent abnormal bone resorption. There is no mention of any subject-matter associated with inhibiting abnormal bone resorption.

4.2.2 The definition of "abnormal bone resorption" in the patent application as filed is (see page 11, lines 18 to 22):

"The term "abnormal bone resorption", as used herein means a degree of bone resorption that exceeds the degree of bone formation, either locally, or in the skeleton as a whole. Alternatively, "abnormal bone

resorption" can be associated with the formation of bone having an abnormal structure."

In the cited "alternative" an inhibition could make sense in meaning inhibition of the formation of bone having an abnormal structure. But this alternative does not refer to osteoporosis but to Paget's disease (see page 14, lines 28 to 30).

An "inhibition" of the "degree of bone resorption that exceeds the degree of bone formation", however, makes no sense from the meaning of the words, and in the absence of a definition in the application would be open to artificial interpretation.

Thus, by introducing "for inhibiting abnormal bone resorption" into claim 1, a feature unknown to the patent application as filed has been created and the combination of "inhibiting" and "abnormal bone resorption" refers to subject-matter extending the content of the patent application as filed.

5. In these circumstances, the arguments of the appellant cannot succeed:

The appellant submitted that for the person skilled in the art the teaching of the patent application as filed was the same as the teaching of the patent after introducing the amendments in each claim 1 and therefore the amended patent contained no subject-matter that extended beyond the content of the patent application as filed.

Particularly, in the wording "for inhibiting bone resorption to treat osteoporosis in a human in need thereof" the reference that "inhibiting bone resorption" was directed to "treating osteoporosis" implied that nothing else would occur than what occurs whenever alendronic acid is used for treating osteoporosis.

In the present case, however, from the different definitions of the "objects of the invention" and from the different definitions of the therapeutic applications in the patent application as filed it is clear that the applicant intended a very specific meaning for these terms. Sometimes the intended meaning does not even meet the normal definition which the skilled person *prima facie* sees in it, for instance with the definition of "abnormal bone resorption" with respect to its "alternative" (see page 11, lines 18 to 22, of the patent application as filed together with point 4.2.2 of this decision).

Under these circumstances, the additional introduction of any of the terms from the patent application as filed in order to define the therapeutic applications for which the medicament has to be manufactured in claim 1 of the main request and of the first to fourth auxiliary requests must be seen as linking their meaning while it was separated before the introduction. This is not simply the addition of a comment which the person skilled in the art would have introduced blindly using his common general knowledge without changing anything, but it is the addition of subject-matter that under Article 123(2) EPC extends beyond the content of the patent application as filed.

6. Accordingly, claim 1 of the main request as well as claim 1 of each of the first to ninth auxiliary requests contravene Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

A. Townend

U. Oswald