

Internal distribution code:

- (A) [] Publication in OJ
(B) [] To Chairmen and Members
(C) [X] To Chairmen
(D) [] No distribution

**Datasheet for the decision
of 12 April 2011**

Case Number: T 1710/09 - 3.3.02

Application Number: 01201913.9

Publication Number: 1175904

IPC: A61K 31/663

Language of the proceedings: EN

Title of invention:

Alendronate for use in the treatment of osteoporosis

Patentee:

Merck Sharp & Dohme Corp.

Opponents:

PLIVA, Farmaceutska Industrija Dionicko Drustvo + AWD.pharma
GmbH & Co. KG
STADA Arzneimittel AG
Hexal AG + Sandoz AG
Arrow International Ltd.
betapharm Arzneimittel GmbH
ZAKLADY FARMACEUTYCZNE POLPHARMA S.A.
Gedeon Richter Plc.
Generics [UK] Ltd. et al
STADA Arzneimittel GmbH
"Interpharm" ProduktionsgmbH
BIOGARAN
Tecnimede, Sociedade Tecnico-Medicinal, S.A.
ACTAVIS GROUP

Headword:

Alendronate for osteoporosis/MERCK

Relevant legal provisions:

EPC Art. 76(1)

Relevant legal provisions (EPC 1973):

-

Keyword:

"All requests: added subject-matter (yes)"

Decisions cited:

T 1138/04, T 0783/09, T 0012/81

Catchword:

-



Case Number: T 1710/09 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 12 April 2011

Appellant: Merck Sharp & Dohme Corp.
(Patent Proprietor) 126 East Lincoln Avenue
Rahway
NJ 07065 (US)

Representative: Horgan, James Michael Frederic
Merck & Co., Inc.
European Patent Department
Merck Sharpe & Dohme Limited
Hertford Road
Hoddesdon
Hertfordshire EN11 9BU (GB)

(Opponent 03) PLIVA, Farmaceutska Industrija Dionicko
Drustvo +
AWD.pharma GmbH & Co. KG
Ulica grada Vukovara 49
Wasastr. 50
HR-10000 Zagreb (HR)/ D-01445 Radebeul (DE)

Representative: Bublak, Wolfgang
Bardehle Pagenberg
Galileiplatz 1
D-81679 München (DE)

(Opponent 04) STADA Arzneimittel AG
Stadastrasse 2-18
D-61118 Bad Vilbel (DE)

Representative: Hamm, Volker
Maiwald Patentanwalts GmbH
Jungfernstieg 38
D-20354 Hamburg (DE)

(Opponent 05) Hexal AG +
Sandoz AG
Industriestrasse 25 / Lichtstrasse 35
D-83607 Holzkirchen (DE)/ CH-4056 Basel (CH)

Representative: Hamm, Volker
Maiwald Patentanwalts GmbH
Jungfernstieg 38
D-20354 Hamburg (DE)

(Opponent 06) Arrow International Ltd.
57 St. Cristopher Street
MT-Valletta (MT)

Representative: Best, Michael
Lederer & Keller
patentanwälte
Unsöldstrasse 2
D-80538 München (DE)

(Opponent 07) betapharm Arzneimittel GmbH
Kobelweg 95
D-86167 Augsburg (DE)

Representative: Hamm, Volker
Maiwald Patentanwalts GmbH
Jungfernstieg 38
D-20354 Hamburg (DE)

(Opponent 08) ZAKLADY FARMACEUTYCZNE POLPHARMA S.A.
ul. Peplinska 19
PL-83-200 Starogard Gdanski (PL)

Representative: Krekora, Magdalena
ul. Gorna 95
PL-32-091 Michalowice (PL)

(Opponent 09) Gedeon Richter Plc.
Gyömrői út 19-21
HU-1103 Budapest (HU)

Representative: Kindler, Matthias
Hoffmann . Eitle
Patent- und Rechtsanwälte
Arabellastrasse 4
D-81925 München (DE)

(Opponent 10) Generics [UK] Ltd. et al
Arcana Arzneimittel GmbH, 1147 Wien (AT)
Merck Generiques, 69008 Lyon (FR)
Qualimed, 69369 Lyon (FR)
Albany Gate, Darkes Lane, Potters Bar
Hertforshire EN6 1AG (GB)

Representative: Jump, Timothy John Simon
Venner, Shipley LLP
20 Little Britain
London EC1A 7DH (GB)

(Opponent 13) STADA Arzneimittel GmbH
Muthgasse 36
AT-1190 Wien (AT)

Representative: Haffner, Thomas M.
Haffner und Keschmann
Patentanwälte OG
Schottengasse 3a
AT-1014 Wien (AT)

(Opponent 14) "Interpharm" ProduktionsgmbH
Effingergasse 21
AT-1160 Wien (AT)

Representative: Schwarz, Albin
Schwarz & Partner
Patentanwälte
Wipplingerstraße 30
AT-1010 Wien (AT)

(Opponent 15) BIOGARAN
15 Boulevard Charles de Gaulle
F-92707 Colombes Cedex (FR)

Representative: Dossmann, Gérard
Casalonga & Partners
Bayerstrasse 71-73
D-80335 München (DE)

(Opponent 16) Tecnimede
Sociedade Tecnico-Medicinal, S.A.
Rua Professor Henrique de Barros
Edificio Sagres, 3 A
PT-2685-338 Prior Velho (PT)

Representative: Engelhard, Elisabeth
Hoffmann . Eitle
Arabellastrasse 4
D-81925 München (DE)

(Opponent 17) ACTAVIS GROUP
Reykjavikurvegur 76-78
IS-222 Hafnarfjordur (IS)

Representative: Klusmann, Peter
Hoffmann . Eitle
Patent- und Rechtsanwälte
Arabellastrasse 4
D-81925 München (DE)

Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted 7 July 2009
revoking European patent No. 1175904 pursuant
to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
 L. Bühler
 A. Lindner
 J.-P. Seitz

Summary of Facts and Submissions

- I. European application No. 01 201 913.9 was granted as European patent No. 1 175 904, the patent in suit, with six claims.

This application is a divisional of application No. 98 935 752.0, which was originally filed as PCT/US98/14796, published without any amendments as WO99/04773-A2 and granted as European patent No. 0 998 292. This (earlier) patent was revoked on 14 March 2006 (T 1138/04, not published in the Official Journal).

The patent in suit was originally filed in the form of said WO99/04773-A2 as the basis of the divisional application.

Independent claim 1 as granted read as follows:

"Use of alendronate in the manufacture of a medicament for treating osteoporosis in a human in need of such treatment, where said medicament is orally administered to said human as a unit dosage comprising about 70 mg of the alendronate compound, on an alendronic acid active weight basis, according to a continuous schedule having a once-weekly dosing interval."

- II. Opposition was filed against the granted patent under Article 100(a) EPC (novelty and inventive step), Article 100(b) EPC (sufficiency of disclosure) and Article 100(c) EPC (added subject-matter).

III. By its decision pronounced at oral proceedings on 18 March 2009 and posted on 7 July 2009, the opposition division revoked the patent under Article 101(3)(b) EPC.

The opposition division held that neither the set of claims of the main request nor that of the auxiliary request met the requirements of Article 56 EPC.

IV. The appellant lodged an appeal against that decision and filed grounds of appeal together with a request that the patent be maintained according to its main request (patent as granted) or to one of its first to fifth auxiliary requests. The second auxiliary request corresponded to the main request before the opposition division.

V. Having withdrawn their oppositions, opponents 01, 02, 11 and 12 were no longer parties to this appeal.

VI. On 12 April 2011, oral proceedings took place before the Board; duly summoned, opponent 03 had informed the Board in advance that it did not wish to attend.

VII. At the beginning of the proceedings, the appellant withdrew its main and first and third auxiliary requests filed with the statement of grounds of appeal. The appellant requested that its former second auxiliary request be considered its new main request, and its former fourth and fifth auxiliary requests its new first and second auxiliary requests.

Claim 1 of the main request reads as follows
(amendments compared to claim 1 as granted in bold):

"Use of alendronate in the manufacture of a medicament for treating osteoporosis in a human in need of such treatment, where said medicament is orally administered to said human **in the form of a tablet** as a unit dosage comprising about 70 mg of the alendronate compound, on an alendronic acid active weight basis, according to a continuous schedule having a once-weekly dosing interval."

Claim 1 of the first auxiliary request is worded like claim 1 of the main request, with the alendronate compound being specified as alendronate monosodium trihydrate. Its wording is (amendments compared to claim 1 of the main request in bold) as follows:

"Use of alendronate **monosodium trihydrate** in the manufacture of a medicament for treating osteoporosis in a human in need of such treatment, where said medicament is orally administered to said human in the form of a tablet as a unit dosage comprising about 70 mg of ~~the~~ alendronate **monosodium trihydrate compound**, on an alendronic acid active weight basis, according to a continuous schedule having a once-weekly dosing interval."

In claim 1 of the second auxiliary request, additionally, after the word "schedule", the words "for at least one year and" are inserted.

VIII. The appellant's submissions may be summarised as follows:

The decision of the opposition division was right in its conclusion that the subject-matter of the requests

met the requirements of Articles 76, 123, 83, 84 and 54 EPC.

With respect to Article 76(1) EPC, all features of the claims as requested were to be found in the application as originally filed in the earlier application.

The combination of the features followed the principle that the person skilled in the art would seriously contemplate the resulting teaching as presented in the current claims.

Thus, claim 1 of the main request could be derived from the paragraph bridging pages 20 and 21, together with page 19 or example 2 respectively.

With respect to the auxiliary requests, the additional feature of the alendronate being monosodium trihydrate was derived in particular from example 2, from original claim 8 or from line 14 on page 19.

The feature "for at least one year" in the second auxiliary request was disclosed in example 2 together with the feature "in the form of a tablet".

Regarding claims 6 to 11 of the earlier application as starting point for the original disclosure of claims 1 of the auxiliary requests, in particular claim 8 together with claims 7 and 6, it was important to see claims 8, 9, 10 and 11 (relating to different dosing intervals) independently from one another and each of them standing alone. As a consequence, the teaching of claims 6 to 8 could be supplemented by the feature "in the form of a tablet" from example 2 or from page 19.

In addition, the "form of a tablet" and the 70 mg of alendronate once-weekly for treatment (as opposed to prevention) of osteoporosis, in particular were presented as preferred features from the overall content of the earlier application. Moreover, the once-weekly dosing interval was in specific correlation to the experiments under example 1.

The mentioning of "alendronate tablets or liquid formulations" under the header "once-weekly dosing regimen" in example 2 provided for disclosure of all alendronates (not only monosodium salt trihydrate) in connection with the medicament in form of tablets on the one hand and made clear on the other hand that "tablet" as one of only two formulations - tablet or liquid - was meant as the preferred embodiment per se. Above that, the tablet was the primarily exemplified form of the medicament in the application as originally filed.

Alendronate in general, not only as monosodium salt trihydrate, was mentioned in addition under example 7 on lines 28 to 30 in connection with differing amounts of active substance in the tablets.

Finally, derivation of a teaching from two lists was allowed according to recent decision T 783/09.

IX. The respondents' arguments may be summarised as follows:

Contrary to the opinion of the opposition division and to the submissions of the appellant, there were

problems with respect to Articles 76(1), 100(c) or 123(2) EPC respectively concerning the requests on file.

In particular, their teaching represented a combination of individually disclosed features which was not allowed in the context as realised in the present claims.

X. The appellant (patentee) requested that the decision under appeal be set aside and the patent be maintained as amended according to the claim set filed as main request, or, in the alternative, according to one of the claim sets filed as first and second auxiliary request during oral proceedings.

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

Reasons for the decision

1. The appeal is admissible.

2. The claims remaining in the proceedings as main and first and second auxiliary requests being no longer objected to by the respondents, and the Board raising no objections of its own motion, are admitted into the proceedings.

3. *Claim 1 of the main request; Article 76(1) EPC*

3.1 This claim 1 relates to the
- use of alendronate ...

- for treating osteoporosis ... orally administered ... in the form of a tablet
- as a unit dosage comprising about 70 mg of the alendronate compound ...
- according to a continuous schedule having a once-weekly dosing interval.

3.2 A combination of claims 6, 7 and 8 as originally filed in the earlier application provides for a combination of these features with the exception of the "form of a tablet", which is missing. Moreover, the active ingredient "alendronate" is disclosed only in the form of the specific salt alendronate monosodium trihydrate and not as alendronate in general. Thus, regarding original claims 6 to 8, the teaching of claim 1 of the main request is at least generalised in an unallowable manner with respect to the active ingredient.

Looking at the description, the missing feature "in the form of a tablet" is found to be mentioned in example 2 together with "alendronate". However, example 2 refers to examples 7 and 8 defining the "alendronate" as monosodium salt trihydrate, because the text in example 2

*"Alendronate tablets or liquid formulations ... **are prepared (see Examples 7 and 8). The tablets ... are orally administered ..."** (emphasis added by the Board)*

leaves no freedom of interpretation that example 2 could relate to another alendronate than the monosodium salt trihydrate actually used (see table under "Example 7" on page 33 as disclosed in W099/04773-A2 which represents the earlier application as originally filed).

If, as an alternative, page 19, lines 18 to 27 are referred to in order to provide a basis for the feature "in the form of a tablet" in claim 1 of the main request, *prima facie* there would be no problem of unallowable generalisation. In these lines 18 to 27, the "form of a tablet" is correlated to bisphosphonates in general. However, in these lines alendronates as the particular embodiment of bisphosphonates are not disclosed for formulation as a tablet. In addition, the form of a tablet is mentioned as only one possibility of various oral forms, together with capsules, elixirs, syrups ... or powder.

To provide a source for allowing the selection of alendronate from bisphosphonates, lines 7 to 14 on the same page could be cited disclosing

- preferred bisphosphonates, *inter alia* alendronate,
- more preferred alendronate, pharmaceutically acceptable salts thereof, and mixtures thereof (potentially meaning the same as alendronate in general) and, however,
- most preferred alendronate monosodium trihydrate.

The only information that is given for answering the question as to what level of preference might be combined with which member of the group of oral forms, e.g. with elixir, powder or in fact tablets, could be that "most preferred" prevails, but in this case the already described problem of unallowable generalisation reappears and claim 1 of the main request is still in breach of Article 76(1) EPC.

3.3 As an alternative, an attempt to find a disclosure of the features of claim 1 of the main request could be started from page 20, line 28 to page 21, line 19 of the description as filed in the earlier application:

- a) The teaching set out there relates to the
- use of alendronate ...
 - as a unit dosage comprising from about 8.75 mg to about 140 mg of the alendronate compound ... (page 20, lines 30 to 32)
 - according to a continuous schedule having
 - a once-weekly dosing interval (page 20, line 33 to page 21, line 4) or
 - a twice-weekly dosing interval (page 21, lines 5 to 11) or
 - a biweekly (page 21, lines 12 to 19) or
 - a twice-monthly dosing interval (page 21, lines 12 to 19)
 - for
 - osteoporosis prevention or
 - treating osteoporosiswith differing unit dosages, namely 35 mg for "prevention" or 70 mg for "treatment" (see page 21, lines 1 to 4, lines 7 to 11 and lines 14 to 19).

The feature "in the form of a tablet" is missing here too.

b) For adding this feature, again example 2 could be referred to:

The teaching of example 2 on pages 29 and 30 of the original application reiterates the two alternatives as being treatment (with 70 mg of alendronate) or prevention of osteoporosis (with 35 mg of alendronate) and in addition discloses two further alternatives as the basis for orally administering 70 mg of alendronate to a human patient once-weekly, namely

- tablets or
- liquid formulations

as exemplified in examples 7 and 8.

c) Thus, reading these sources of disclosure relevant for the subject-matter as requested in claim 1 of the main request, the skilled person is free in principle to combine different variations of the elements being suggested as features of the claim with respect to

- dosage (e.g. **70 mg**),
- dosing interval (e.g. **once-weekly**) and
- form of the formulation (e.g. **in the form of a tablet**),

with no recognisable preference for the features as actually represented in this claim (indicated in bold).

d) Reference to page 19 instead of example 2 also cannot solve the problem of providing for the feature "in the form of a tablet" (and not as a syrup or elixir etc.) clearly connected to alendronate in general (not to monosodium trihydrate) and at the same time clarifying the preference of "once-weekly" and the dosage of 70 mg, as can be seen from the arguments under point 3.2, fourth paragraph *et seq.* above.

3.4 As a consequence, a unit dosage of **70 mg** of alendronate **in the form of a tablet** for a **once-weekly** dosing interval for **treating** osteoporosis is not individualised in the description as originally filed in the earlier application, and the subject-matter of claim 1 of the main request cannot be derived directly and unambiguously.

3.5 First and second auxiliary request; Article 76(1) EPC

3.5.1 The considerations and conclusions under point 3.3 above apply *mutatis mutandis* to claims 1 of the first and second auxiliary requests because, as the core amendment, they differ only in restriction from alendronate to monosodium trihydrate (with the additional wording that the medicament was orally administered to the human "for at least one year" in the second auxiliary request). These considerations in particular are valid for starting from pages 20 and 21 of the description as originally filed.

3.5.2 With respect to the claims as originally filed in the earlier application as the basis for the original disclosure, it is to be stressed that they equally reflect a) the structure of the teaching of pages 20/21, b) the structure of the description and c) the structure of the examples.

In these three cases a), b) and c), the alternatives for

- the dosage,
differ in relation to the use, mostly

- 35 mg (osteoporosis prevention) or
- 70 mg (treating osteoporosis)
(see claims 12, 13 and 14 or 6, 7 and 8 respectively
or see page 21, lines 1 to 4, lines 7 to 11 and
lines 14 to 19 or see sub-headings of examples 2, 3,
4 and 5),

- the alternatives for the dosing interval
are
 - a once-weekly dosing interval (see claims 8 and
14 or see page 20, line 33 to page 21, line 4 or
example 2) or
 - a twice-weekly dosing interval (see claims 9 and
15 or see page 21, lines 5 to 11 or example 3)
or
 - a biweekly (see claims 10 and 16 or see page 21,
lines 12 to 19 or example 4) or
 - a twice-monthly dosing interval (see claims 11
and 17 or see page 21, lines 12 to 19 or
example 5).

This teaching is to be supplemented for the form of the
formulation

- from the examples representing as alternatives,
 - tablets or
 - liquid formulations
(see the alternatives presented in examples 2, 3, 4
and 5)

- or from page 19 presenting, as alternatives,
 - tablets, capsules, elixirs, syrups, effervescent
compositions, powders, and the like or
 - tablet, capsule, or powder

respectively (see page 19, lines 22 to 23 or line 25).

In all cases, the alternatives are of equal weight, no preference is indicated by specific words or in any other directly recognisable way and their singling out for reasons of original disclosure is not allowed.

3.5.3 Therefore, also when starting from the claims as originally filed, the particular combination of features in claim 1 of the first and the second auxiliary requests is not to be found in individualised form in the earlier application as originally filed and the provisions of Article 76(1) EPC are not fulfilled.

4. Under these circumstances, the additional arguments of the appellant cannot hold.

4.1 Applying the principle of direct and unambiguous derivability gives rise to a clear and unequivocal conclusion in the present case. There is no room for any question as to what the skilled person would seriously contemplate.

4.2 The "form of a tablet" as well as "70 mg of alendronate once-weekly for treatment of osteoporosis" as preferred features in view of the overall content of the earlier application could not be seen by the Board, and specific and convincing arguments for this opinion were not presented.

For instance, it is not apparent why the structure of the experiments of example 1 would indicate particular weight being attached to a once-weekly dosing: on

page 27, lines 10 to 14 of the description of the earlier application it is set out that considerably less oesophageal irritation was observed from the administration of a single high concentration of alendronate on a weekly basis (Group 5) **or twice-weekly basis (Group 6)** versus administration of low concentration dosages on consecutive days (Group 2) (emphasis added by the Board), giving once-weekly the same weight as twice-weekly.

With respect to the other arguments of the appellant, it is to be stated that in view of example 8 the tablet form is not the primarily exemplified form of the medicament in the application as originally filed, and the mentioning of the word "alendronate" in example 7 does not alter the fact that only the "monosodium salt trihydrate" is specifically used in this example.

- 4.3 Coming to its conclusion, the present Board duly considered decision T 783/09 of 25 January 2011 (not published in the Official Journal) cited by the appellant in support of its line of argumentation concerning the disclosure in its originally filed application of the features currently claimed. With respect to T 12/81, the following is emphasised in T 783/09:

"... given the term "can" in the citation from decision T 12/81, the absence of a direct and unambiguous disclosure for individualised subject-matter is not a mandatory consequence of its presentation as elements of lists. Thus, the "disclosure status" of subject-matter individualised from lists has to be determined according to the circumstances of each specific case by

ultimately answering the question whether or not the skilled person would clearly and unambiguously derive the subject-matter at issue from the document as a whole" (reasons, point 5.6; underlining by this Board).

While it is stressed in T 783/09 that the circumstances of each specific case are decisive for the outcome of the assessment of the "disclosure status", it follows from points 3.3 and 3.5 above, in particular point 3.3 c), that the specific circumstances of the present case are different from those considered in T 783/09 and nothing has been submitted during the proceedings that might justify a statement to the contrary.

Thus, complying fully with the issue "disclosure status" to be uniformly assessed in all cases of entitlement to priority or original disclosure of an amendment on the one hand and novelty of a claimed subject-matter on the other hand in answering to the question *"whether or not the skilled person would clearly and unambiguously derive the subject-matter at issue from the document as a whole"*, the present Board considers it inappropriate to expand all the reasonings and conclusions with respect to the particular subject-matter of decision T 783/09 to the present case. The present Board adheres to the meaning of the sentence in seminal decision T 12/81 "If on the other hand two classes of starting substances are required to prepare the end products and examples of individual entities in each class are given in two lists of some length, then a substance resulting from the reaction of a specific pair from the two lists can nevertheless be regarded for patent purposes as a selection and hence as new."

(underlining by this board) taking "can" for a "is to" as the therefrom following standing jurisprudence did. In view of the implications of freely interpreting this word "can", there is deep concern that in this way the uniformity of the disclosure assessment process cannot be warranted.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

N. Maslin

U. Oswald