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**Datasheet for the decision
of 22 November 2010**

Case Number: T 0451/07 - 3.3.02

Application Number: 98907038.8

Publication Number: 0969813

IPC: A61K 9/06

Language of the proceedings: EN

Title of invention:

Topical pharmaceutical composition comprising a cholinergic agent or a calcium channel blocker

Patentee:

S.L.A. Pharma AG

Opponent:

Tecnimedede Sociedade Tecnico-Medicinal, S.A.

Headword:

Topical composition for anorectal pain/S.L.A. Pharma

Relevant legal provisions:

EPC Art. 54

Relevant legal provisions (EPC 1973):

-

Keyword:

"Novelty (no): Anticipated by preferred embodiment of the state of the Art"

Decisions cited:

-

Catchword:

-



Case Number: T 0451/07 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 22 November 2010

Appellant:
(Patent Proprietor)

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Decision under appeal:

Decision of the Opposition Division of the
European Patent Office posted 22 February 2007
revoking European patent No. 0969813 pursuant
to Article 102(1) EPC 1973.

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
J. Van Moer

Summary of Facts and Submissions

- I. European patent No. 0 969 813, based on international application PCT/GB1998/000575, published as WO 1998/036733 and having application No. 98 907 038.8 in the EPO, was granted with 27 claims.

Independent claims 1 and 9 as granted read as follows:

"1. A composition adapted for topical application in and around the anal canal for the treatment or prophylaxis of benign anal disorders associated with high anal pressure or anal sphincter spasm comprising diltiazem or a pharmaceutically acceptable salt thereof and bethanechol or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier.

9. Use of diltiazem or a pharmaceutically acceptable salt thereof in the preparation of a medicament for topical application in and around the anal canal for the treatment or prophylaxis of benign anal disorders associated with high anal pressure or anal sphincter spasm."

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

The documents cited during the proceedings before the opposition division and the board of appeal include the following:

(1) WO-A1-95/06466

(9) Reynolds, J.; Martindale, The Extra Pharmacopoeia, 31st Ed. (1996), 784-788, 857-859, 874-877, 916-921

III. By its decision posted on 22 February 2007, the opposition division revoked the patent under Article 102(1) and (3) EPC 1973.

The opposition division held that the sets of claims of the main request and auxiliary requests 1 to 3 met the requirements of Articles 123(2) and 83 EPC.

However, the subject-matter of independent claim 9 of each of the main request and the auxiliary requests 1 and 2 as well as of independent claim 1 of auxiliary request 3 was not novel with regard to document (1).

Auxiliary request 4 was refused as late-filed.

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 or its first to fourth auxiliary requests, all requests being the same as those made during the proceedings before the opposition division.

The sets of claims of the main request and the first and second auxiliary requests were filed during the opposition proceedings with letter dated 16 February 2006.

Claims 9 of the main request and the first auxiliary request and claim 1 of the third auxiliary request are

identical to claim 9 as granted (according to point III, first paragraph, in the decision of the opposition division and to its Annex 4, the third auxiliary request was filed during the opposition proceedings with letter dated 7 November 2006).

In claim 9 of the second auxiliary request, with respect to the main request, the diseases to be treated are restricted to "haemorrhoids or anal fissures" (amendments in bold below):

"9. Use of diltiazem or a pharmaceutically acceptable salt thereof in the preparation of a medicament for topical application in and around the anal canal for the treatment or prophylaxis of **haemorrhoids or anal fissures.**"

Claim 9 of the fourth auxiliary request was filed with letter dated 25 January 2007 during the proceedings before the opposition division (see Annex 5 of the decision of the opposition division). It relates to the percentage of diltiazem in the medicament in the form of a range; the request is worded as follows (added text in bold):

"9. Use of diltiazem or a pharmaceutically acceptable salt thereof in the preparation of a medicament for topical application in and around the anal canal for the treatment or prophylaxis of benign anal disorders associated with high anal pressure or anal sphincter spasm, **wherein the medicament contains diltiazem or a pharmaceutically acceptable salt thereof in an amount of 1% to 5% w/w.**"

V. On 22 November 2010, oral proceedings took place before the board.

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

From the mechanism postulated in document (1) with respect to activating NO-production, the person skilled in the art would have recognised a contradiction in NO-synthase enzyme needing calcium-ions on the one hand and diltiazem being a calcium channel blocker on the other hand. Therefore he would have ruled out the specific use of diltiazem for treating anorectal disorders as suggested *inter alia* by the teaching of document (1).

In addition, the teaching of document (1) comprised nearly all possible ways of administering of an active ingredient. The preferred application "directly to the anus" at least left open whether to administer topically or by direct injection.

Moreover, the skilled person would have been deterred from considering diltiazem as a possible active ingredient for topical administration, because such administration - particularly as a medicament of approved activity and inoffensiveness - was not known from a common text book such as document (9); on the contrary, from this text book diltiazem was known to cause skin irritation when given orally.

Finally, there was only one substance set out as an example for treatment of anal disorders in document (1) and this example concerned the NO-producing substance

nitroglycerine, and not a vasodilator such as diltiazem in topical administration.

Thus, from the technical reality represented by document (1), despite diltiazem being mentioned in a list, the person skilled in the art would not have considered it for topical use for treatment of anorectal disorders.

At least, there was no clear and unambiguous disclosure to use diltiazem for topical administration for the treatment or prophylaxis of benign anal disorders associated with high anal pressure or anal sphincter spasm as claimed in the patent in suit.

With respect to claim 9 of the fourth auxiliary request, the selection of a particular range for the content of diltiazem in the medicament provided novelty to the claimed teaching since it was fundamentally restricted from the range set out in document (1). Even diltiazem already had to be selected from a list of recommended active ingredients and the topical administration route was disclosed only as one possibility amongst others too.

VII. The respondent's arguments may be summarised as follows:

The teaching of document (1) was to use substances that mediate either directly or indirectly relaxation of the anal sphincter, for instance diltiazem, to treat anorectal disorders, in particular haemorrhoids and anal fissure in humans. With respect to a list of ways of administration, a treatment "directly to the anus" was preferred. Considering this preference in relation

to the list could only result in concluding that the topical one was the preferred way of administration meant.

Thus, the teaching of the independent use-claims of the main request and the first to third auxiliary request was anticipated by document (1), just as the opposition division had already decided.

The range for the content of diltiazem in the medicament as set out in claim 9 of the fourth auxiliary request overlapped with that disclosed in document (1), so this feature as claimed lacked novelty too.

VIII. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the set of claims filed as main request or the first or second auxiliary request filed with letter dated 16 February 2006 or alternatively on the basis of the set of claims filed as the third auxiliary request with letter dated 7 November 2006 or the fourth auxiliary request filed with letter dated 25 January 2007.

IX. The respondent (opponent) requested that the appeal be dismissed.

Reasons for the decision

1. The appeal is admissible.
2. The decision of the opposition division referred to anticipation of the claimed teaching with respect to document (1) (Article 54 EPC).
3. *Claim 9 of the main request; Article 54 EPC*
 - 3.1 The subject-matter of this claim essentially relates to the
 - use of diltiazem in the preparation of a medicament
 - for topical application in and around the anal canal
 - for the treatment or prophylaxis of benign anal disorders associated with high anal pressure or anal sphincter spasm.

Specific examples for the disorders to be treated are haemorrhoids and anal fissures (see claims 26 and 27 of the main request).
 - 3.2 The teaching of document (1) is related to
 - the treatment of anorectal disorders, in particular haemorrhoids and anal fissures (see page 1, lines 4 to 7)
 - by administering the active ingredients of the invention orally, "topically", parenterally or by inhalation; preferably directly to the anus (see page 5, lines 9 to 12, in particular lines 11 to 12),
 - the active ingredient being selected from a list comprising diltiazem (see page 4, line 22).

The list of ways of administration in document (1) originally reads: ... orally, topically, transdermally, parenterally such as by direct injection into the site of anorectal pain, by inhalation, transdermally, intrarectally, or to tissue surrounding the anus.

The wording "topically, transdermally, intrarectally, or to tissue surrounding the anus" means nothing else than "topically" as defined in the patent in suit, since from its paragraph [0037], "Pharmaceutical compositions adapted for topical administration in and/or around the anal canal may be formulated as ointments, creams, suspensions, lotions, powders, solutions, pastes, gels, sprays, foam, oils, aerosols, suppositories or enemas". The use of suppositories, for instance, corresponds to the intrarectal way of administration and thus is understood to be comprised by the term topical administration while transdermally is also a variant of topical administration from the common general knowledge of the skilled person.

Considering the remainder of the list of ways of administration, by preferring "directly to the anus",

- "orally",
- "parenterally", and
- "by inhalation"

are to be excluded, leaving "topically" as the only alternative in the sense of the patent in suit.

Parenterally is ruled out because any injection to veins or muscles or subcutaneous injection is comprised at any site of the body. "Such as" in this context

indicates only an arbitrary example which therefore is to be excluded together with the more general term.

Thus, there is clear and unambiguous teaching that document (1) relates to the treatment of anorectal disorders, in particular haemorrhoids and anal fissures, by administering the active ingredients of the invention directly to the anus, which means topically.

As one of the active ingredients to be used in this treatment, diltiazem is to be found in a list of suggested substances (see document (1), page 4, line 22).

- 3.3 In accordance with the jurisprudence of the boards that every active ingredient contained in one list to be used in such a treatment represents a teaching that is fully disclosed as an individualised embodiment, the topical use of diltiazem to treat anorectal diseases like haemorrhoids and anal fissures as disclosed in document (1) anticipates the teaching of claim 9 of the main request.
4. Claim 9 of the first auxiliary request and claim 1 of the third auxiliary request are worded identically and cannot be novel either.
5. *Claim 9 of the second auxiliary request; Article 54 EPC*

Compared to the main request, the additional feature of claim 9 of the second auxiliary request is the specific definition of the disease as "haemorrhoids or anal fissures". Since the treatment of these specific diseases is also provided in document (1) (see

point 3.2 of this decision), the teaching of the second auxiliary request is also not new.

6. *Claim 9 of the fourth auxiliary request; Article 54 EPC*

With respect to claim 9 of the second auxiliary request, the additional feature of claim 9 of the fourth auxiliary request is the specific definition of the range of content of diltiazem in the medicament as an amount of 1% to 5% w/w.

The upper limit of this range is identical to the upper limit provided in document (1) for the presence of the active ingredient in the composition (see line 22 on page 5).

Therefore the amount of active ingredient to be used in its upper limit is anticipated by the teaching of document (1), and the subject-matter of claim 9 of the fourth auxiliary request also lacks novelty over this document.

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

The argument that safe topical use of diltiazem was not known from the textbook (9), meant to represent common general knowledge, does not provide proof or evidence that a skilled person would have either totally excluded diltiazem with respect to topical application or would have excluded diltiazem from the probability of exerting any effect on anal sphincter pressure. Known irritations of the skin under oral administration

are not indicative for effects generated by topical administration in general.

Therefore, the teaching of document (1) is not affected by this argumentation. In document (1), diltiazem is exemplified as a substance to be used and on page 4, lines 19 to 21 reasons are given why the effect in treatment of haemorrhoids and anal fissures is to be expected, namely because "any vasodilator compound ... which relaxes the anal sphincter may be used in this invention".

Moreover, there is no indication in the entire document that the topical route was restricted to compounds other than diltiazem, e.g. to nitrate compounds, or that there could be any considerations that diltiazem was excluded from the topical way of administration for any other reason. Even that there is only one example and the medicament in this example does not represent a vasodilator is no proof or indication that the other active substances mentioned in the document would not work.

- 7.1 With respect to the possible mechanisms as indicated in document (1), it is to be pointed out that this part of document (1) refers to the action of substances that as far as known mediate NO-concentrations in smooth muscles, for instance in activating NO-production from L-arginine (see in particular page 3, lines 2 to 5). These mechanisms are not meant to apply to all the substances considered to be suitable to treat anorectal pain. Thus, there is no internal contradiction in document (1) with NO-synthase enzyme needing calcium-ions on the one hand and diltiazem being a calcium

channel blocker on the other hand. Diltiazem was contemplated as a promising active ingredient because of being a vasodilator which was known to relax the anal sphincter and there was no indication of any connection to NO-synthase in document (1).

7.2 All these arguments together show that there is no "technical reality" in contradiction to the teaching of document (1) which would deter the skilled person from accepting it just as it is presented in the international application.

7.3 The range indicated in claim 9 of the fourth auxiliary request for the content of diltiazem in the medicament is disclosed in document (1) with an identical figure for the upper limit (5%) and overlapping the whole extent of range, down to the lower limit as claimed (1%) (see document (1), page 5, lines 21 to 23). Thus, there is no selection of range in the claimed teaching with respect to document (1).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

S. Louca-Dreher

U. Oswald