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Datasheet for the decision of 1 October 2009

Case Number: T 0601/07 - 3.3.02

Application Number: 01947305.7

Publication Number: 1284711

IPC: A61J 1/03

Language of the proceedings: EN

Title of invention:
Process for making a blister package containing topiramate tablets

Patentee:
Cilag AG

Opponent:
Actavis Group hf.

Headword:
Blister package containing topiramate tablets/CILAG AG

Relevant legal provisions:
EPC Art. 54, 56

Keyword:
"Main request: novelty - (no): Product not rendered novel by its method of preparation"
"Auxiliary requests 1 - 5: inventive step - (no)"
"Auxiliary request 6: inventive step - (yes): alternative process for preparing blister packages containing topiramate tablets not obvious"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0601/07 **-** 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 1 October 2009

Appellant: (Opponent)
Actavis Group hf.
Actavis Group hf.
Reykjavikurvegur 76-78
IS-220 Hafnarfjordur (IS)

Representative:
Vossius & Partner
Siebertstraße 4
D-81675 München (DE)

Respondent: (Patent Proprietor)
Cilag AG
Hochstrasse 201
CH-8205 Schaffhausen (CH)

Representative:
Fisher, Adrian John
CARPMAELS & RANSFORD
43-45 Bloomsbury Square
London WC1A 2RA (GB)

Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 12 February 2007 rejecting the opposition filed against European Patent No. 1284711 pursuant to Article 102(2) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: A. Lindner
J. Van Moer

Summary of Facts and Submissions

I. European patent No. 1 284 711 based on application No. 01 947 305.7 was granted on the basis of a set of 11 claims.

Independent claims 1 and 11 and dependent claims 9 and 10 read as follows:

"1. A process for making a blister package containing topiramate tablets comprising the steps of:

(a) drying a plurality of topiramate tablets to a free water content of between about 0.4% to about 1.4%;

(b) placing the dried topiramate tablets from step (a) into a pan sheet having a plurality of cavities; and

(c) sealing a cover sheet to the pan sheet from step (b) to form the blister package, provided that the dried topiramate tablets have a free water content of less than about 1.4% at the time the cover sheet is sealed to the pan sheet and wherein the blister package contains no desiccant.

9. The process of claim 1 wherein the topiramate tablets are dried by a method selected from the group consisting of microwave drying, vacuum drying, hot air drying, infrared drying, drying using very dry air either statically or dynamically, and drying by placing a desiccant in a storage drum of bulk product for a period of time.

10. The process of claim 9 wherein the topiramate tablets are dried using hot air in a coater at a temperature from about 60°C to about 70°C.

11. A blister package made by the process of claim 10."

II. An opposition was filed against the granted patent. The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step.

III. The documents cited during the opposition and appeal proceedings included the following:

(1b) Marketing Approval of BfArM for Topomax including page 16 filed by the patentee with letter dated 6 June 2006
(2) WO 99/44581

IV. In the decision pronounced on 15 November 2006, the opposition division rejected the opposition. Its principal findings were as follows:

As regards novelty, none of the available prior art documents clearly and unambiguously disclosed topiramate tablets with a free water content of between about 0.4 to about 1.4%. As for inventive step, neither of documents (1b) and (2) referred to the problem of limiting the content of free water in the topiramate formulations or tablets to increase its stability to a level which permits packaging without a desiccant.

V. The appellant (opponent) lodged an appeal against that decision.

VI. With his reply to the statement of the grounds of appeal dated 6 November 2007, the respondent (patentee) filed auxiliary requests 1 to 3.

VII. Oral proceedings took place on 1 October 2009. At the oral proceedings, the respondent filed auxiliary requests 1 to 9. The independent claims read as follows:

(a) auxiliary request 1:

"1. A process for making a blister package containing topiramate tablets comprising the steps of:

(a) drying a plurality of topiramate tablets to a free water content of between 0.4% to 1.4%;

(b) placing the dried topiramate tablets from step (a) into a pan sheet having a plurality of cavities; and

(c) sealing a cover sheet to the pan sheet from step (b) to form the blister package, provided that the dried topiramate tablets have a free water content of less than 1.4% at the time the cover sheet is sealed to the pan sheet and wherein the blister package contains no desiccant."

(b) auxiliary request 2:

"1. A process for making a blister package containing topiramate tablets comprising the steps of:

(a) drying a plurality of topiramate tablets to a free water content of between 0.4% to 1.4%;

(b) placing the dried topiramate tablets from step (a) into a pan sheet having a plurality of cavities, wherein the pan sheet is a composite metal and plastic layer; and

(c) sealing a cover sheet to the pan sheet from step (b) to form the blister package, wherein the cover sheet is a metal layer, provided that the dried

topiramate tablets have a free water content of less than 1.4% at the time the cover sheet is sealed to the pan sheet and wherein the blister package contains no desiccant."

(c) auxiliary request 3:

"1. A process for making a blister package containing topiramate tablets consisting of the steps of:

(a) drying a plurality of topiramate tablets to a free water content of between 0.4% to 1.4%;

(b) placing the dried topiramate tablets from step (a) into a pan sheet having a plurality of cavities; and

(c) sealing a cover sheet to the pan sheet from step (b) to form the blister package, provided that the dried topiramate tablets have a free water content of less than 1.4% at the time the cover sheet is sealed to the pan sheet and wherein the blister package contains no desiccant.

11. A blister package made by the process of claim 10."

(d) auxiliary request 4:

The sole independent claim 1 is identical to claim 1 of auxiliary request 3.

(e) auxiliary request 5:

The sole independent claim 1 is identical to claim 1 of auxiliary request 2 except for the replacement of "comprising" by "consisting of".

(f) auxiliary request 6:

"1. A process for making a blister package containing topiramate tablets comprising the steps of:

(a) drying a plurality of topiramate tablets to a free water content of between 0.4% to 1.4%;

(b) placing the dried topiramate tablets from step (a) into a pan sheet having a plurality of cavities, wherein the pan sheet is a composite metal and plastic layer of ortho-polyamide/aluminum foil/polyvinylchloride; and

(c) sealing a cover sheet to the pan sheet from step (b) to form the blister package, wherein the cover sheet is a single aluminum foil layer, provided that the dried topiramate tablets have a free water content of less than 1.4% at the time the cover sheet is sealed to the pan sheet and wherein the blister package contains no desiccant."

(g) auxiliary request 7:

The sole independent claim 1 is identical to claim 1 of auxiliary request 6 except for the replacement of "comprising" by "consisting of".

(h) auxiliary request 8:

"1. A process for making a blister package containing topiramate tablets comprising the steps of:

(a) drying a plurality of topiramate tablets to a free water content of between 0.4% to 1.4%;

(b) placing the dried topiramate tablets from step (a) into a pan sheet having a plurality of cavities,

wherein the pan sheet is a 25µm ortho-polyamide/ 45µm aluminum foil/60µm polyvinylchloride sheet; and

(c) sealing a cover sheet to the pan sheet from step (b) to form the blister package, wherein the cover sheet is a single 20µm aluminum foil sheet, provided that the dried topiramate tablets have a free water content of less than 1.4% at the time the cover sheet is sealed to the pan sheet and wherein the blister package contains no desiccant."

(i) auxiliary request 9:
The sole independent claim 1 is identical to claim 1 of auxiliary request 8 except for the replacement of "comprising" by "consisting of".

VIII. The appellant's arguments can be summarised as follows:

In connection with novelty, it was reasoned that both the process according to claim 1 and the blister package defined by its process for preparation lacked novelty over document (1b) in view of the fact that it was impossible to distinguish between a residual water content of about 1.7% (document (1b)) and less than about 1.4% (contested patent).

As regards inventive step, document (1b), which disclosed blister packages comprising topiramate tablets, wherein two blister packages were sealed into a pouch containing a desiccant, was defined as the closest prior art. The only difference between the disclosure of document (1b) and the process as claimed in the contested patent was the moisture content that

was not specifically mentioned in document (1b). As the contested patent itself contained data which showed that the products obtainable by a process according to the present invention were less stable than the products of document (1b), the problem to be solved merely concerned the provision of a further process for preparing blister packages containing topiramate tablets. The problem was solved by eliminating the desiccant and by drying the tablets to a residual free water content of less than 1.4%. No inventive step could be seen in measures sacrificing stability for ease of preparation. Moreover, the drying step was obvious in the light of document (1b), which contained the information that the topiramate tablets had to be protected from moisture.

IX. The respondent held that the product claimed in the main request was novel, as document (1b) did not disclose the residual moisture content of the topiramate tablets. In connection with inventive step, document (1b), which disclosed a stable but very expensive product in the form of a blister in pouch composition, constituted the closest prior art. The function of the desiccant in document (1b) was to prevent the entry of moisture, but this effect disappeared once the pouch was opened. There was no hint in the available prior art that topiramate tablets could be stably stored in blister packages in the absence of a desiccant.

X. The appellant requested that the decision under appeal be set aside and that the European patent be revoked.

The respondent requested that the appeal be dismissed or, in the alternative, that the patent be maintained on the basis of any of auxiliary requests 1 to 9 submitted during the oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. *Admissibility of auxiliary requests 1 to 9:*

These requests were filed only at an advanced stage of the oral proceedings before the board. However, as they were a reaction by the respondent to arguments presented for the first time at the oral proceedings, and were such that the appellant was not taken by surprise, the board decided to admit them (Article 13 RPBA).

3. *Main request - novelty of claim 11:*

Claim 11 relates to a product defined by its method of preparation. As repeatedly decided by boards of appeal, "product-by-process" claims have to be interpreted in an absolute sense, i.e. independently of the process. They have thus to be examined like any other product claim, namely as to whether or not the claimed product fulfils the basic requirements of novelty (Article 54 EPC) and inventive step (Article 56 EPC).

In the present case, the subject-matter of claim 11 comprises every blister package obtainable by a process

according to claim 1 in combination with claims 9 and 10, no matter how the blister package was prepared.

For the evaluation of novelty, it therefore appears essential to examine whether any of the process features are transferred to the product obtainable by the process and, if so, which. It is of particular interest in the present case to verify whether the free water content constitutes a feature of the claimed product.

According to step (a) of present claim 1, the topiramate tablets are dried to a free water content of between 0.4 and 1.4%, then they are placed into a pan sheet (step (b) and finally, the cover sheet is added. At the time the cover sheet is sealed to the pan sheet, the topiramate tablets have a free water content of less than 1.4% (step (c)).

In view of the fact that both the pan sheet and the cover sheet may be made of any material including a non-water-resistant material and bearing in mind that claim 1 is an open claim, i.e. a claim that may comprise further steps in addition to steps (a), (b) and (c) such as a simple resting step during which the topiramate tablets may absorb some water, the board arrived at the conclusion that the free water content does not constitute a limiting feature for the product of present claim 11. It is additionally noted that dependent claims 9 and 10, to which claim 11 refers, are directed to further details concerning the drying step, which do not have a limiting character for the product, either. As a consequence, the subject-matter of "product-by-process claim" 11 includes any blister

package comprising a pan sheet and a cover which contains topiramate tablets and no desiccant.

Document (1b) discloses "Topamax" products comprising topiramate tablets in blister packages comprising a pan sheet made of PE/PVDC/PVC and a cover sheet in the form of a 20 µm aluminum foil. Two blister packages are sealed in a pouch comprising a desiccant (see pages 1 and 16).

In view of the fact that the disclaimer (see claim 1) only excludes blister packages where the package itself contains a desiccant, packages where two desiccant-free blisters are contained in a pouch comprising a desiccant are included in present claim 11. As a consequence, the subject-matter of claim 11 of the main request is not novel over the blister packages of document (1b). The requirements of Article 54 EPC are therefore not met.

In the light of this finding, the assessment of novelty of claim 1 is not necessary.

4. *Auxiliary request 1:*

4.1 Novelty of claim 1:

As mentioned in point 3 above, document (1b) discloses blister packages comprising topiramate tablets, wherein two blisters are sealed in a pouch comprising a desiccant. Document (1b) does not specifically disclose the preparation of these blister packages. In particular, document (1b) does not disclose the step of drying the topiramate tablets to a free water content

of between 0.4 to 1.4% (step (a) of present claim 1). As a consequence, the subject-matter of claim 1 is novel (Article 54 EPC).

4.2 Inventive step of claim 1:

4.2.1 According to the description of the contested patent, the present invention concerns a process for making a blister package containing topiramate tablets, wherein the tablets are protected from degradation (see pages 2, lines 9 and 26-30 of the contested patent). Before the closest prior art can be defined, it appears necessary to evaluate whether the subject-matter of claim 1 in its entirety is directed to a process for preparing blister packages in which the topiramate is effectively protected from exposure to moisture, which is the primary cause of degradation.

4.2.2 Example 3 of the contested patent concerns a blister package evaluation study in which topiramate tablets having a free water content of about 1.7% were packaged in various package formats. Composition 2 of example 3 concerns a blister package having an OPA/Alu/PVC (25µm/45µm/60µm) pan sheet and a hard aluminum foil (20 µm) cover sheet, while the blister package of composition 5 is characterised by a PVC/PE/PVDC (200µm/25µm/90g/m^2) pan sheet and a hard aluminum foil (20 µm) cover sheet. The subsequent evaluation study shows that composition 2 is much more effective in retarding degradation of topiramate than composition 5 (see paragraphs [0040] and [0043] of the contested patent). Although the products of example 3 were not prepared according to a process as defined in present claim 1, in view of the fact that the topiramate

tablets were not dried to a free water content of between 0.4-1.4%, example 3 nevertheless demonstrates convincingly that, in order to achieve adequate protection against degradation, it is not sufficient to dry the topiramate tablets to a very low residual water content before they are sealed into the blister package. It is also necessary to select a wall material for both the cover and the pan sheets that provides an effective barrier against incoming humidity. As present claim 1 includes any blister package, the board concludes that the present invention as defined in claim 1 simply concerns the provision of blister packages containing topiramate tablets.

4.2.3 Document (1b), which constitutes the closest prior art, relates to blister packages containing topiramate tablets, which, as already mentioned in point 3 above, are protected from degradation in that two blister packages are enclosed in a pouch which additionally contains a desiccant. The blister packages themselves do not contain a desiccant. They comprise a pan sheet made of PE/PVDC/PVC and a cover sheet in the form of a 20 µm aluminum foil sheet (see pages 1 and 16).

4.2.4 Accordingly, the technical problem to be solved is the provision of a process for making further blister packages containing topiramate tablets, which was solved by a process according to the present claim 1. In view of the examples, in particular example 4, the board is satisfied that the problem has indeed been plausibly solved.

4.2.5 Document (1b) does not disclose the residual water content of the topiramate tablets. As a consequence, it

discloses neither that the topiramate tablets are dried to a free water content of between 0.4 and 1.4% (step (a) of present claim 1) nor that the dried topiramate tablets have a free water content of less than 1.4% at the time the cover sheet is sealed to the pan sheet (step (c) of present claim 1). Document (1b) does, however, contain the information that the topiramate tablets should be protected against humidity (see page 18: "Vor Feuchtigkeit schützen"). In the light of this teaching, it would appear obvious to dry the tablets to a low residual water content and to seal them into the blister package in that dry state. Such a step cannot involve an inventive step. It therefore remains to evaluate whether the specific selection of the ranges for the residual water content (0.4-1.4% in step (a) and less than 1.4% in step (c)), as such, causes a non-obvious effect on which an inventive step could be based.

4.2.6 As already explained in paragraph 4.2.2 above, drying the topiramate tablets to a residual water content of 0.4-1.4% and sealing them into the blister package in that dry state in itself does not result in enhanced stability, as long as the material of the pan and cover sheets is not selected so as to provide an effective barrier against humidity, which is not the case in present claim 1. In view of the fact that no effect can be attributed to the ranges for the residual water content, their selection does not involve an inventive step. As a consequence, the subject-matter of claim 1 does not meet the requirements of Article 56 EPC.

5. *Auxiliary request 2 - inventive step of claim 1:*

Claim 1 of auxiliary request 2 differs from claim 1 of auxiliary request 1 in that the pan sheet is now made of a composite material and a plastic layer and the cover sheet is a metal layer. As in the examples (see examples 3 and 4) only blister packages comprising OPA/Alu/PVC (pan sheet) and a hard aluminum foil (cover sheet) are shown to provide an effective barrier against humidity, the board came to the conclusion that in the absence of evidence to the contrary not every pan sheet comprising an unspecified plastic layer and an unspecified metal layer and every cover sheet comprising an unspecified composite metal, as claimed in claim 1 of auxiliary request 2, is effective against incoming humidity. As a consequence, the reasoning of paragraph 4.2 in connection with inventive step of claim 1 of auxiliary request 1 applies ***mutatis mutandis*** to claim 1 of auxiliary request 2. The requirements of Article 56 EPC are therefore not met.

6. *Auxiliary request 3 - inventive step of claim 1:*

Claim 1 of auxiliary request 3 differs from claim 1 of auxiliary request 1 in that "comprising" is replaced by "consisting of". However, the exclusion of additional process steps does not change the reasoning in connection with inventive step as compared to auxiliary request 1. As a consequence, the reasoning of paragraph 4.2 in connection with inventive step of claim 1 of auxiliary request 1 applies ***mutatis mutandis*** to claim 1 of auxiliary request 3. The requirements of Article 56 EPC are therefore not met.

7. *Auxiliary request 4 - inventive step of claim 1:*

Claim 1 of auxiliary request 4 is identical to claim 1 of auxiliary request 3. As a consequence, the reasoning of paragraph 6 above applies to present claim 1. The requirements of Article 56 EPC are therefore not met.

8. *Auxiliary request 5 - inventive step of claim 1:*

Claim 1 of auxiliary request 5 differs from claim 1 of auxiliary request 2 in that "comprising" is replaced by "consisting of". However, the exclusion of additional process steps does not change the reasoning in connection with inventive step as compared to auxiliary request 2. As a consequence, the reasoning of paragraph 5 in connection with the inventive step of claim 1 of auxiliary request 2 applies ***mutatis mutandis*** to claim 1 of auxiliary request 5. The requirements of Article 56 EPC are therefore not met.

9. *Auxiliary request 6 - inventive step of claim 1:*

9.1 Claim 1 of auxiliary request 6 differs from claim 1 of auxiliary request 1 in that the pan sheet is now made of a composite material and a plastic layer of ortho-polyamide/aluminum foil/polyvinylchloride and the cover sheet is a single aluminum foil layer.

Document (1b) remains the closest prior art. As for the blister packages disclosed in document (1b), see paragraph 4.2.3 above.

9.2 With regard to this prior art, the technical problem to be solved is the provision of an alternative process,

i.e. the provision of a process which yields topiramate tablets, whose stability is in practical terms comparable to the stability of tablets of document (1b). To determine whether the problem has been plausibly solved by changing the composition of the pan sheet from PE/PVDC/PVC to ortho-polyamide/aluminum foil/polyvinylchloride and by drying the topiramate tablets in steps (a) and (c) to a free water content as defined in present claim 1, it is necessary to evaluate the data of the test examples in the contested patent.

Example 4 concerns a blister package evaluation study in which topiramate tablets having a free water content of about (a) 0.8%, (b) 1.4% or (c) 1.8% were sealed into a blister package having an ortho-polyamide/aluminum foil/polyvinylchloride (25µm/45µm/60µm) pan sheet and a hard aluminum foil (20µm) cover sheet. Batches (b) and (c) are comparative examples, given that the free water content of the topiramate tablet has to be **less than** 1.4% according to step (c) of present claim 1. The evaluation study demonstrates that the blister packages of batch (a), which are according to the invention claimed in present claim 1, meet the appearance specification for 36 months at 30°C/60° RH and for 18 months at 40°C/75% RH (see page 9, line 36 to page 10, line 12 and table 7 of the contested patent). As a consequence, the blister packages of batch (a) comply with the Guidelines of the International Committee on Harmonization, which require tablets to be maintained within approved specifications under accelerated stability conditions of 40°C/75 RH at least six months (see page 9, lines 19-21 of the contested patent). As a consequence, the board is convinced that the problem has been plausibly solved.

9.3 Starting from document (1b) as closest prior art, the skilled person has no incentive to change the composition of the pan sheet and to dry the tablets in steps (a) and (c) to the required residual water content in order to arrive at an alternative process for preparing stable topiramate tablets. As a consequence, the subject-matter of auxiliary request 6 meets the requirements of Article 56 EPC.

9.4 Additional arguments of the appellant:

9.4.1 The subject-matter of claim 1 of auxiliary request 6 did not relate to an alternative process for preparing blister packages containing stable topiramate tablets, but only to a further process for preparing blister packages comprising topiramate tablets, in view of the fact that the products according to claim 1 of auxiliary request 6 were less stable than the products of document (1b). In this context, reference was made to composition 3 of example 3, which concerned a product according to document (1b) and to composition 1 of example 4 of the contested patent, which related to a blister package obtainable by a process as defined by the present claims and to the corresponding appearance specification data in the contested patent (see paragraph [0041] and table 7).

9.4.2 It is correct that the appearance specification data mentioned above demonstrate an enhanced stability of composition 3 of example 3 as compared to composition 1 of example 4. However, document (1b) does not disclose the residual water content of the topiramate tablets. In example 3 of the contested patent, commercially

available topiramate tablets with a residual water content of about 1.7% were used and, in the case of composition 3, sealed into a blister package having the same composition as the blister package of document (1b) (see paragraph [0035] of the contested patent). However, in view of the fact that the residual water content of the topiramate tablets of document (1b) is not known, composition 3 of example 3 is not truly representative of the blister packages according to document (1b). As a consequence, no conclusions can be drawn as regards the stability of the blister packages according to document (1b). This argument therefore cannot succeed.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to maintain the patent with the following documents:

   1. claims 1 to 6 of the sixth auxiliary request.
   2. a description to be adapted.

The Registrar: The Chairman:

N. Maslin U. Oswald