Internal distribution code:

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

Datasheet for the decision of 16 October 2014

Case Number: T 1007/10 - 3.3.01

Application Number: 03770970.6

Publication Number: 1608362

IPC: A61K31/40

Language of the proceedings: EN

Title of invention:
STABILIZED PHARMACEUTICAL PREPARATION COMPRISING AN AMORPHOUS ACTIVE SUBSTANCE

Patent Proprietor:
LEK Pharmaceuticals d.d.

Opponent:
Miklich Laboratorios SA

Headword:
Packaging in inert gas/LEK

Relevant legal provisions:
EPC Art. 56
RPBA Art. 13

Keyword:
Inventive step - (no)

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern
Boards of Appeal
Chambres de recours

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 1007/10 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 16 October 2014

Appellant: (Patent Proprietor)	LEK Pharmaceuticals d.d. Verovskova 57 1526 Ljubljana (SI)
Representative:	TBK Bavariaring 4-6 80336 München (DE)
Appellant: (Opponent 3)	Miklich Laboratorios SA Cuevas Bajas s/n - Of. 23 Edificio Picasso 29004 Malaga (ES)
Representative:	Nohlen, Martin Uexküll & Stolberg, Patentanwälte Beselerstrasse 4 22607 Hamburg (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 31 March 2010 concerning maintenance of the European Patent No. 1608362 in amended form.**

Composition of the Board:

Chairman	A. Lindner
Members:	L. Seymour
	L. Bühler

Summary of Facts and Submissions

I. European patent No. 1 608 362 was filed on 10 October 2003 and claims priority of 11 October 2002. The claims as granted consist of twenty-five claims. Independent claims 1, 13 and 19 read as follows:

"1. A pharmaceutical preparation comprising a pharmaceutical formulation with amorphous atorvastatin calcium exposed to an inert gas atmosphere.

...

13. A method for stabilization of a pharmaceutical formulation comprising amorphous atorvastatin calcium and pharmaceutically acceptable excipients, wherein the pharmaceutical formulation is stored in an inert atmosphere.

...

19. A method of stabilization of amorphous atorvastatin calcium, wherein the amorphous atorvastatin calcium is stored in an inert atmosphere."

II. Three oppositions were filed and revocation of the patent in its entirety requested pursuant to Articles 100(b) and 100(a) EPC, for lack of novelty and inventive step. *Inter alia* the following documents were submitted in opposition proceedings:

(3) WO 02/072073

(11) WO 01/93859

(12) US-A-5 686 104

(14) K C Waterman et al., Pharm. Dev. Technol., January 2002, 7(1), 1 - 32

(15) WO 97/03958

(16) WO 97/03959

(18) Pharmaceutical Dosage Forms, H A Lieberman and L Lachman (eds.), Marcel Dekker, vol. 1, 1980, 38; vol. 3, 1982, 356 - 365

(19) Physicochemical Principles of Pharmacy, A T Florence and D Attwood, Pharmaceutical Press, 3rd edition, 1998, 103 - 105

(28) EP-A-1 241 110

(39) EP-B-1 653 930

(40) WO 2005/011638

III. The appeals lie from the interlocutory decision of the opposition division maintaining the patent in amended form based on auxiliary request 1 filed during the oral proceedings before the opposition division. The subject-matter claimed was found to meet the requirements of the EPC, and, in particular, to involve an inventive step in the light of document (3) as closest prior art.

IV. The patent proprietor and opponents 1 to 3 each lodged an appeal against this decision. Subsequently, with letters of 22 March 2012 and 30 September 2014, respectively, the then appellant opponents 1 and 2 withdrew their oppositions and appeals and lost, as a

consequence, their party status. Therefore, in this decision, "the appellant opponent" refers to opponent 3.

V. With letter dated 29 April 2011, the appellant patentee filed auxiliary requests 1 to 4.

Auxiliary request 1 differs from the claims as granted (main request, cf. above point I) in the insertion of the adjective "stable" into the product claims (i.e. claims 1 to 7).

Auxiliary request 2 is identical to auxiliary request 1 considered in the decision under appeal (cf. above point III). Independent claim 5 of this request is identical to independent claim 19 as granted (cf. above point I).

Auxiliary request 3 differs from auxiliary request 2 in the insertion of the adjective "stable" into the product claims (i.e. claims 1 to 4).

Claim 1 of auxiliary request 4 is identical to independent claim 19 as granted.

VI. In a communication dated 24 March 2014, sent as annex to the summons to oral proceedings, the board *inter alia* drew the parties' attention to a number issues relating to the entitlements to priority of the patent in suit and of two intermediate documents (39) and (40), and to the possible consequences thereof for the assessment of novelty.

VII. With its response dated 23 May 2014, the appellant patentee filed auxiliary requests A to E, each consisting of a single claim.

Claim 1 of auxiliary request A differs from claim 1 as granted (cf. above point I) in the insertion of the following feature at the end of the claim:

"wherein the formulation is in a substantially gas-exchange non-permeable package, wherein the package is an Al/Al blister".

In claim 1 of auxiliary request B, this additional feature is modified to read:

"wherein the pharmaceutical formulation comprises amorphous atorvastatin calcium and pharmaceutically acceptable excipients, wherein the pharmaceutical formulation is stored in an inert atmosphere in an Al/Al blister".

Claim 1 of auxiliary request C differs from claim 13 as granted (cf. above point I) in insertion of the following feature at the end of the claim:

"wherein the formulation is packed into a gas non-permeable package, wherein the gas non-permeable package is selected from the group consisting of Al/Al blister, Al—polychloro—3—fluoroethylene homopolymer/PVC laminate blister or a bottle".

Auxiliary request D is based on auxiliary request C with an additional limitation in claim 1 that "the gas non-permeable package is an Al/Al blister".

Auxiliary request E is based on auxiliary request D, wherein the inert atmosphere has been defined to be "nitrogen or argon".

VIII. Following the appellant opponent's letter of 15 September 2014, the appellant patentee filed auxiliary requests Aa and Ab, and Ba and Bb with letter of 10 October 2014, which only differ from auxiliary Requests A and B, respectively, in the addition of dependent claims.

IX. Oral proceedings were held before the board on 16 October 2014.

X. The appellant opponent's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

All the appellant patentee's requests submitted after the summons to oral proceedings, that is, auxiliary requests A to E and Aa to Bb, should not be admitted into the proceedings. The board's preliminary opinion of 24 March 2014 was an inadequate excuse for the late filing of these requests. Documents (39) and (40) had been filed during the first instance proceedings, and the issue of priority had also been discussed. The appellant opponent further criticised the number of newly filed requests, their lack of clear allowability, and the fact that some of the requests related to method claims whereas the decision under appeal had focused on product claims.

In its assessment of inventive step, the appellant opponent accepted that document (3) could be seen as the closest prior art. This document disclosed pharmaceutical formulations containing atorvastatin calcium in amorphous form, and suggested the addition of a basic or buffering agent as a means of stabilisation. No comparison had been provided demonstrating an improvement with respect to this

document. Therefore, the problem to be solved was to be seen as lying in the provision of alternative methods for stabilising amorphous atorvastatin calcium and pharmaceutical formulations thereof, and of corresponding pharmaceutical preparations.
Document (11) disclosed that, in order to further reduce the carbon dioxide content and thus further improve stability of such pharmaceutical formulations, it was useful to package them under a nitrogen atmosphere. In addition, document (11) taught the use of blister and airtight packages. It was irrelevant that document (11) did not discuss the sensitivity of atorvastatin to oxygen, since, by following its teaching, the skilled person would arrive at the subject-matter claimed. The latter did not exclude the use of a combination of methods of stabilisation, as suggested in document (11).

Moreover, the sensitivity of amorphous atorvastatin towards oxygen was known at the effective date of the patent in suit, as confirmed in documents (15) and (16). The skilled person would also have been aware of well-known measures for protecting oxygen-sensitive drugs from degradation, such as the use of inert gas atmospheres as disclosed in documents (14), (18) and (19). More specifically, document (14) taught packaging under nitrogen or argon to reduce the headspace oxygen, in particular, for solid dosage forms packaged in blisters, such as foil-foil blisters. Reference was further made to document (28) as disclosing the use of aluminum as a foil material in blister packaging. Therefore, the more specific embodiments claimed in the auxiliary requests were also rendered obvious by the teaching of these documents.

XI. The appellant patentee's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

The filing of requests A to E was to be seen as direct response to the board's preliminary assessment of the disclosures of document (39) and (40). The additional auxiliary requests Aa to Bb had been filed in order to address the appellant opponent's objections under Rule 80 EPC, raised in its letter of of 15 September 2014. Although numerous, the requests could be dealt with without difficulty, since they were all based on the same inventive concept relating to the packaging and stabilisation of amorphous atorvastatin calcium under an inert gas atmosphere. These requests should therefore be admitted into the proceedings.

With respect to the issue of inventive step, the appellant patentee started from document (3) as the closest prior art. This disclosed amorphous atorvastatin calcium in the form of tablets. The problem to be solved was to be seen as lying in the provision of a pharmaceutical preparation comprising amorphous atorvastatin calcium which was stable, as well as a method of stabilising amorphous atorvastatin calcium. The solution as defined in the claims was characterised in that the amorphous atorvastatin calcium was provided under inert gas atmosphere. The examples of the patent in suit demonstrated that amorphous atorvastatin calcium, in pure form or in tablets, could be stabilised by using nitrogen or argon.

None of the cited prior art hinted at the present solution to the problem posed.

Document (3) itself related to a totally different problem than the patent in suit, namely, on achieving pharmaceutical formulations which would be therapeutically equivalent regardless of whether atorvastatin calcium was present in crystalline or amorphous form.

Similarly, the focus of document (11) was on the sensitivity of statins to pH, and on their stabilisation by addition of substances neutralising carbon dioxide. Furthermore, the examples all related to pravastatin, and there was no disclosure of amorphous atorvastatin calcium therein. The purpose of using a nitrogen atmosphere as disclosed in document (11) was to further reduce carbon dioxide content in the package, and this measure was considered to be insufficient on its own. Additionally, the passage on page 9 of document (11) could be interpreted in such a way that only the separate element or compartment containing the carbon dioxide binding and/or neutralizing substance was packed under the nitrogen atmosphere. Nowhere was it stated that the atmosphere surrounding the pharmaceutical formulation was also to be replaced by nitrogen, as in the patent in suit.

There was no indication in documents (3) or (11) that amorphous atorvastatin calcium was an oxygen-sensitive substance. Indeed, at the effective date of the patent in suit, amorphous atorvastatin calcium had not been tested or found to be highly sensitive to oxygen. The skilled person would therefore have no motivation to combine these documents with further documents dealing with methods for stabilising pharmaceuticals from oxidative degradation, such as documents (14), (18) or (19). Rather, he would have expected that routine methods, such as the use of antioxidants, as suggested

in document (12), would be sufficient to prevent any oxidation encountered, and this would have been his first choice.

In this context, the appellant patentee referred to example 6 of document (39) as post-published evidence, and the finding therein in relation to amorphous atorvastatin calcium that "the use of antioxidants, routinely used in the pharmaceutical industry, does not prevent oxidation processes in the dosage form". In view of these negative results, the skilled person would not have investigated further methods of oxidative stabilisation in the expectation of producing a stable product.

Certainly, there would be no motivation for the skilled person to turn to the much more complicated procedure of packaging under an inert gas atmosphere. This had not been a standard procedure at the time, as confirmed in document (14). Here, numerous possibilities for stabilisation to oxidation were disclosed, and packaging under nitrogen was the very last approach addressed, and was described as being cumbersome. This document therefore taught away from the present solution. These arguments were all the more relevant to claimed embodiments relating to Al/Al blisters, since document (14) listed several drawbacks in relation to blister packaging in general, and only disclosed blister packaging under nitrogen and argon as being "sometimes feasible ... to reduce headspace oxygen".

Finally, according to documents (15) and (16), amorphous atorvastatin calcium had unsuitable filtration and drying characteristics for large-scale production, and had to be protected from heat, light, oxygen, and moisture. The solution proposed in these

documents in order to address these disadvantages was the preparation of crystalline forms. These documents therefore taught away from using the amorphous form of atorvastatin.

A further indication that the subject-matter claimed involved an inventive step could be derived from the considerable time that had elapsed between the first disclosure of amorphous atorvastatin calcium and the present invention.

XII. The appellant patentee requested that the decision under appeal be set aside and that the patent be maintained as granted (main request), or, alternatively, on the basis of:

- auxiliary request A filed with letter of 23 May 2014,
- auxiliary requests Aa or Ab filed with letter of 10 October 2014,
- auxiliary request B filed with letter of 23 May 2014,
- auxiliary requests Ba or Bb filed with letter of 10 October 2014, or
- auxiliary request 1 filed with letter of 29 April 2011,

or, alternatively, that the appeal of the appellant opponent be dismissed (auxiliary request 2),
or, alternatively, that the decision under appeal be set aside and that the patent be maintained on the basis of:

- auxiliary requests C, D or E filed with letter of 23 May 2014, or
- auxiliary requests 3 or 4 filed with letter of 29 April 2011.

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

XIII. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Admission of auxiliary requests A to E and Aa to Bb into appeal proceedings*

The amendments undertaken in requests A to E and Aa to Bb with respect to requests previously on file are readily identifiable as a straightforward reaction to a communication of the board and a letter of the appellant opponent (cf. above points VI to VIII, respectively). Since the specific objections raised therein, by the board with respect to documents (39) and (40) and by the appellant opponent pursuant to Rule 80 EPC, had not been previously addressed, it is only fair that the appellant patentee be given the opportunity to react in an appropriate manner. In the present case, auxiliary requests A to E and Aa to Bb related to subject-matter that was based on combinations of claims as granted. They did not result in a change in the nature of the debate and could be discussed without delay. The board therefore decided to admit these requests into the proceedings (Article 13(1) RPBA).

3. *Main request - Inventive step (Articles 52(1), 56 EPC)*

3.1 Although the claim set as granted comprises additional independent claims (claims 8 and 25), for reasons of conciseness, the analysis below concentrates on independent claims 1, 13 and 19 (cf. above point I), since they are also to be found in a number of the auxiliary requests, or form the basis for corresponding claims present therein (cf. above points V and VII).

Claim 19 is directed to a method for stabilising amorphous atorvastatin calcium. Claim 13 relates to a corresponding method for stabilising a pharmaceutical formulation comprising amorphous atorvastatin calcium. In both cases, the methods are characterised in that the products are "stored in an inert atmosphere". Claim 1 is a product claim directed to "a pharmaceutical preparation", in which the pharmaceutical formulation is "exposed to an inert gas atmosphere".

There was disagreement between the parties as to the meanings of the terms "inert atmosphere" and "inert gas atmosphere". However, for the purpose of the analysis below, it will be assumed, in favour of the appellant patentee, that these terms are synonymous, and relate to an atmosphere consisting of an inert gas such as nitrogen or argon (cf. dependent claims 6, 14 and 20 as granted). Similarly, "a pharmaceutical preparation" is construed as referring to a packaged pharmaceutical formulation.

3.2 The board considers, in agreement with the parties, that document (3) represents the closest state of the art.

This document relates to pharmaceutical formulations comprising atorvastatin calcium, present in crystalline and/or amorphous form (see claims 7 to 12).

In the introductory section of document (3), it is disclosed that basic or buffering substances were known in the literature to provide stability to atorvastatin calcium formulations, and to the amorphous substance. The relevant passage on page 3, lines 7 to 17 reads as follows (emphasis added):

"The patent literature describes atorvastatin calcium as an unstable substance and offers numerous solutions to provide **a stable atorvastatin pharmaceutical formulation**. Thus, for example, the stability of the formulation can be provided **by the addition of a basic or a buffering agent** to the formulation (WO 00/35425, WO 94/16603), namely by stabilizing the substance according to an analogous method described for pravastatin sodium in the patent application WO 01/93860. In order to prepare a **stabilized amorphous substance**, a combination of the methods disclosed in WO 01/93860, Slovene patent application P-9900271, and WO 01/42209 can be used."

According to the disclosure of document (3), pH adjusting substances of the type outlined above (see e.g. page 5, lines 25 to 35; claim 18) can also be used to achieve pharmaceutical formulations that are therapeutically equivalent regardless of their solid-state form (page 3, lines 24 to 29), by minimising the differences in solubility between amorphous and crystalline atorvastatin calcium (see e.g. page 4, line 24 to page 5, line 4).

In Tables 1 and 4 of document (3) (pages 7 and 8), various pharmaceutical formulations comprising amorphous atorvastatin calcium are disclosed, including examples wherein basic or buffering substances are present or absent (see e.g. Table 1, rows MgO and Na_2HPO_4).

3.3 In view of this state of the art, the problem underlying the patent in suit, as formulated during the oral proceedings before the board, was to provide further methods of stabilising amorphous atorvastatin calcium and pharmaceutical formulations thereof, and to provide a stable pharmaceutical preparation comprising such a pharmaceutical formulation.

3.4 The solution as proposed in claims 1, 13 and 19 relates to storage and packaging in an inert gas atmosphere.

The examples in the patent in suit demonstrate that amorphous atorvastatin calcium (example 1) as well as corresponding tablets (example 2) can be stabilised by using nitrogen 99% (vol/vol). Similarly, tablets packed into blisters with aluminum foil in argon 99% (v/v) were demonstrated to be more stable than those packed in air (example 3).

Having regard to this data, the board is satisfied that the problem has been solved.

For the sake of completeness, it is noted in this context that, in the written proceedings, the appellant patentee asserted various improvements in stability with respect to the prior art, primarily based on post-published document (39) (see letter of 29 April 2011, pages 17/19 and 18/19). However, the cited examples 6 and 8 are neither comparable with one another, nor do

they properly reflect the distinguishing feature of the claimed subject-matter with respect to the closest prior art. Since this line of argumentation was not pursued at oral proceedings, a more detailed reasoning in this respect is not required.

3.5 It remains to be investigated whether the proposed solution would have been obvious to the skilled person in the light of the prior art.

3.5.1 As becomes evident from the analysis under point 3.2 above, document (3) already discloses that atorvastatin calcium formulations, and the amorphous substance can be stabilised in an analogous manner to pravastatin sodium, by employing basic or buffering agents.

Starting from the compositions exemplified in document (3), the skilled person, seeking a solution to the problem defined above, would consult further documents relating to the stabilisation of the present class of HMG-CoA reductase inhibitors. Document (11) is one such document and discloses that atorvastatin, and its calcium salt, like pravastatin and its sodium salt, degrade to the lactone in an acidic environment, caused by the presence of carbon dioxide (see page 2, lines 9 to 14; page 4, line 29 to page 5, line 2; page 10, lines 9 to 13). Stabilisation is achieved by combination with a carbon dioxide binding and/or neutralizing substance; the stabilising agent may be incorporated directly, or provided in separate element or compartment of a pharmaceutical package separated from the active ingredient or the pharmaceutical formulation (see page 7, lines 1 to 31; claims 1 to 3). With respect to the latter option, it is further suggested that, "in producing the pharmaceutical package or administration material according to the

present invention, the separate element or compartment containing the carbon dioxide binding and/or neutralizing substance may be incorporated into the pharmaceutical package or administration material **under nitrogen atmosphere in order to further reduce carbon oxide content"** (page 9, lines 17 to 24, emphasis added).

Therefore, it is concluded that document (11) specifically suggests a packaging process under a nitrogen atmosphere as an additional means of achieving stabilisation. Applying this measure to amorphous atorvastatin calcium and formulations thereof as disclosed in document (3) directly leads the skilled person to products and processes in accordance with claims 1, 13 and 19, without the exercise of inventive skill.

This subject-matter therefore lacks an inventive step with respect to the combined teachings of documents (3) and (11).

3.5.2 Moreover, it is acknowledged in the patent in suit itself that, in addition to its instability to low pH, atorvastatin calcium, particularly in amorphous form, was also known to be susceptible to heat, moisture, and light (see paragraphs [0006], [0007]). This is confirmed in documents (15) and (16), which, however, additionally specify that amorphous atorvastatin calcium must be protected from oxygen (see document (15), page 2, lines 29 to 33, and document (16), page 2, lines 28 to 32; note: in these documents (cf. first paragraph), the term "atorvastatin" is used to designate "atorvastatin calcium"). The skilled person, being aware of this fact, would have had an additional motivation to turn

to standard methods for preventing oxidative degradation, such as storage and packaging under an inert gas atmosphere (see e.g. document (14), page 24, right-hand column, first three paragraphs; document (18), page 38, "Stability to Oxidation", first sentence; document (19), page 105, first paragraph).

3.5.3 The appellant patentee's arguments in favour of inventive step do not hold for the following reasons:

As outlined above in point 3.2, although the focus of document (3) is on providing therapeutically equivalent formulations, it also addresses the problem of achieving stability, which is the problem underlying the patent in suit (cf. above point 3.3). Document (3) cannot therefore be said to be related to a totally different problem than the patent in suit.

Moreover, as explained above in point 3.5.1, stabilisation by storage under an inert gas atmosphere is considered to be an obvious measure in view of the combined teachings of documents (3) and (11). It is not rendered any less obvious by the recognition that, in addition to reducing carbon dioxide content, this measure necessarily results in the elimination of further deleterious environmental factors, such as oxygen. Therefore, the fact that these documents do not deal with the issue of oxygen sensitivity cannot alter the above conclusion.

The appellant patentee further pointed to the fact that the examples of document (11) all related to pravastatin. However, it clearly emerges from documents (3) and (11) that the stability issues in question would also apply to atorvastatin calcium (cf. above points 3.2 and 3.5.1).

Moreover, the appellant patentee argued that, according to document (11), packaging under a nitrogen atmosphere was not sufficient to impart stability. The relevant passage on page 5, lines 2 to 8 reads (see also page 22, lines 1 to 10): "Even if a non-stabilized HMG-CoA reductase inhibitor-containing pharmaceutical formulation is packed under nitrogen atmosphere but was before exposed to normal atmosphere, the pH which would be generated when obtaining an aqueous solution thereof is slowly going down and eventually leads to an increase in impurities and degradation products". However, it cannot be derived from this sentence that packaging under nitrogen is *per se* insufficient, but rather that additional precautions would be required to avoid exposure to a normal atmosphere prior to packaging. Furthermore, this argument is not considered to be relevant for the simple reason that the present claims do not exclude the use of combinations of methods of stabilisation, as advocated on page 9 of document (11). Indeed, in examples 2 and 3 of the patent in suit, the formulations comprise the basifying agent magnesium oxide, in addition to being stored or packed under nitrogen (see paragraphs [0029] and [0032]).

Finally, the appellant patentee submitted with respect to document (11) that the passage on page 9, reproduced above in point 3.5.1, was to be read as referring to the packaging of the separate element and not to the packaging process as a whole. However, it is amply clear from the phrases "in producing the pharmaceutical package" and "incorporated into the pharmaceutical package" that, according to this option, the packaging process as a whole is being described and that it takes place under a nitrogen atmosphere.

Regarding the appellant patentee's assertion that it had not been known at the effective date of the patent in suit that amorphous atorvastatin calcium was an oxygen-sensitive substance, this is not considered to be credible, in view of the explicit disclosures in documents (15) and (16) of the need to protect amorphous atorvastatin calcium from oxygen. Moreover, these documents cannot be considered to teach away from the present invention. Although these documents list several disadvantages associated with the amorphous form, the skilled person would also be aware of a number of advantages relating to its solubility and bioavailability (cf. e.g. patent in suit, paragraphs [0005] and [0007]; and document (3), page 1, lines 27 to 33). Therefore, it cannot be accepted that the skilled person would be dissuaded from further investigating formulations comprising the amorphous form.

Similarly, document (14) cannot be considered to teach away from the present measures. Although packaging under nitrogen is described as being cumbersome on page 24, it is also disclosed as having the advantage that it "can reduce significantly the headspace oxygen". Therefore, this passage merely teaches the need to weigh up the advantages and disadvantages of said option.

The appellant patentee further argued that, if the skilled person had indeed been motivated to protect amorphous atorvastatin calcium from oxygen, he would have attempted the incorporation of antioxidants, as suggested in document (12), and found that it did not produce the desired results (cf. document (39)). However, it does not follow, as argued by the appellant

patentee, that the skilled person would then have abandoned all other solutions offered in the relevant prior art, such as document (14). Indeed, it could rather be argued that the negative results with antioxidants would encourage him to look to other known methods of stabilisation based on different mechanisms, particularly in view of the possibility of undesired interactions between the active ingredient and other additives in a formulation (see e.g. document (11), page 2, lines 16 to 24; document (14), page 22, paragraph bridging left- and right-hand columns).

Finally, the time factor invoked by the appellant patentee cannot in itself form the basis for acknowledging an inventive step, since the timing of the present invention might have resulted from a variety of causes, such as commercial considerations with respect to the packaging procedure.

3.6 In view of the above analysis, the subject-matter of claim 1, 13 and 19 of the main request is found to represent an obvious solution to the problem posed and does not involve an inventive step.

Consequently, the appellant patentee's main request is rejected for lack of inventive step.

4. *Auxiliary requests A, Aa and Ab*

Auxiliary requests A, Aa and Ab each contain identical claims 1, which are based on claim 1 as granted, whereby it has been additionally specified that "the formulation is in a substantially gas-exchange non-permeable package, wherein the package is an Al/Al blister" (cf. above points VII and VIII).

The appellant patentee argued that these additional features further contributed to an inventive step, since the combination of features claimed was not foreshadowed by the prior art.

However, document (11), in the same section as that analysed above in point 3.5.1 (see document (11), page 8, line 19 to page 9, line 36), suggests blister and airtight packaging as being suitable containers for the dosage forms (see specifically page 9, lines 3 and 34).

Moreover, blister packaging is also suggested in document (14), and specifically foil-foil blisters (page 24, right-hand column, third paragraph). The appellant patentee did not dispute that aluminum was known to be a suitable foil material in blister packaging (see document (28), column 7, lines 13 to 16).

Again, document (14) emphasises the advantages (oxygen barrier properties) and disadvantages (cost, opaque) of this type of packaging, and it is in this context that the skilled person would read the last sentence of said paragraph, which states: "It is sometimes feasible to blister package under nitrogen or argon to reduce the headspace oxygen". In other words, "sometimes feasible" cannot be accepted to teach away from adopting the methods disclosed, but merely expresses the need to consider practicability on weighing up the factors previously discussed.

In view of the above, it is concluded that the additional measures introduced into the respective claims 1 cannot impart an inventive step to the subject-matter claimed.

Hence, auxiliary requests A, Aa and Ab are also rejected for lack of inventive step of their respective claims 1.

5. *Auxiliary requests B, Ba and Bb*

Auxiliary requests B, Ba and Bb each contain identical claims 1 (cf. above points VII and VIII). With respect to the requests discussed above in point 4, the amendments were primarily introduced in order to more closely reflect the wording in the priority document (cf. appellant patentee's letter of 23 May 2014, point 2b).

The appellant patentee did not submit any additional arguments in favour of inventive step of these requests. The board also cannot see that the amendments undertaken affect the considerations outlined above in point 4.

Hence, auxiliary requests B, Ba and Bb are also rejected for lack of inventive step of their respective claims 1.

6. *Auxiliary requests C, D and E*

Process claim 1 of auxiliary request D is based on claim 13 of the main request whereby it has been additionally specified that "the formulation is packed into a gas non-permeable package, wherein the gas non-permeable package is an Al/Al blister"; claim 1 of auxiliary request C also encompasses this embodiment (cf. above point VII). Therefore, in substance, these claims have been modified in the same manner as the

product claim 1 of auxiliary request A discussed above in point 4.

In claim 1 of auxiliary request E the inert atmosphere has been further defined to be "nitrogen or argon". However, since the analysis in points 3 and 4 above were based on a reading of "inert atmosphere" that took into account said feature (cf. above point 3.1), this amendment also cannot alter the conclusion reached.

Indeed, the appellant patentee did not submit any additional arguments in favour of inventive step of these requests. Therefore, the reasoning and conclusions detailed in points 3 and 4 apply *mutatis mutandis* to claims 1 of the auxiliary requests C, D and E.

Thus, auxiliary requests C, D and E are not considered to be allowable for lack of inventive step

7. *Auxiliary requests 1 to 4*

Claims 13 and 19 of auxiliary request 1 are identical to claims 13 and 19 of the main request. Similarly, the respective claims 5, 5 and 1 of auxiliary requests 2, 3 and 4 are identical to claim 19 of the main request (cf. above point V). The considerations concerning claims 13 and 19 of the main request, as set out above in point 4, therefore apply equally.

Hence, auxiliary requests 1 to 4 are not allowable for lack of inventive step.

8. *Other issues*

The appellant opponent raised a number of further objections with respect to sufficiency of disclosure and novelty of the requests considered above. In addition, a number of formal objections were brought forward under Articles 84 and 123(2) EPC, and Rule 80 EPC, regarding the amendments to the auxiliary requests. In view of the negative outcome of these appeal proceedings on the question of inventive step, as set out in points 3 to 7 above, a decision of the board on these issues was not necessary.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated