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**Datasheet for the decision
of 17 September 2015**

Case Number: T 2566/11 - 3.3.07

Application Number: 02785879.4

Publication Number: 1465608

IPC: A61K9/50, A61K31/135

Language of the proceedings: EN

Title of invention:

EXTENDED RELEASE COMPOSITIONS COMPRISING AS ACTIVE COMPOUND
VENLAFAXINE HYDROCHLORIDE

Patent Proprietor:

KRKA, tovarna zdravil, d.d., Novo mesto

Opponents:

Alfred E. Tiefenbacher GmbH & Co. KG
Hennig Arzneimittel GmbH & Co. KG
STRAWMAN LIMITED
Wyeth LLC

Relevant legal provisions:

RPBA Art. 12(1), 13(1), 12(4)
EPC 1973 Art. 56

Keyword:

Inventive step -
main request and auxiliary requests 1 to 6 (no)
Auxiliary requests 1 to 6 - admitted (yes)
Late-filed auxiliary requests 7 - admitted (no)



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Case Number: T 2566/11 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 17 September 2015

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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
25 November 2011 concerning maintenance of the
European Patent No. 1465608 in amended form.**

Composition of the Board:

Chairman J. Riolo
Members: A. Usuelli
T. Karamanli

Summary of Facts and Submissions

- I. European patent No. 1 465 608 was granted on the basis of European patent application No. 02785879.4.

Granted claim 1 read as follows:

"1. An extended release composition comprising as active compound Venlafaxine Hydrochloride, in which Venlafaxine Hydrochloride is coated on a non pareil inert core, which coated core is then coated with an isolating/protecting/separating layer, which is then coated with an additional polymeric layer controllably releasing the Venlafaxine Hydrochloride."

- II. Four oppositions were filed against the patent on the grounds that its claimed subject-matter lacked novelty and inventive step, was insufficiently disclosed, and extended beyond the content of the application as filed. The following documents were among those cited during the first-instance proceedings:

D1: WO-A-99/22724

D7: WO-A-01/19901

D14: US 4,786,505

D15: "Aqueous polymeric coatings for pharmaceutical dosage forms", J.W. McGinity, 1997, Chapter 9

D16: "Multiparticulate oral drug delivery", I. Ghebre-Sellassie, 1994, Chapters 5 and 10

D17: Colorcon: Surelease® brochure, October 1990

D22: Experimental data filed by the patent proprietor with letter of 26 September 2011.

- III. By decision posted on 25 November 2011, the opposition division maintained the patent in amended form on the basis of the set of claims according to the first

auxiliary request filed on 26 September 2011. The claims of the main request were the claims as granted.

Claim 1 of the first auxiliary request corresponded to claim 1 as granted, with the following additional text:

".. wherein said composition comprises 0.5-10% of the isolating layer per weight of the total dosage form".

IV. In its decision, the opposition division came to the conclusion that the subject-matter of claim 1 of the main request lacked novelty over a prior-art document pursuant to Article 54(3) EPC.

The subject-matter of claim 1 of the first auxiliary request was considered novel. The requirements of Article 56 EPC were also met. Document D1 was regarded as the closest prior art. The composition of claim 1 differed from the disclosure of D1 in that (i) venlafaxine was coated on a non pareil core, (ii) the coated core was coated with an isolating/protecting/separating layer between the coated core and an additional polymeric layer, and (iii) the composition comprised 0.5-10% of the isolating layer per weight of the total dosage form. The objective technical problem was the provision of an alternative extended release composition of venlafaxine hydrochloride, which allows for a more industrially efficient production and provides bioequivalent release characteristics to the compositions of D1. In order to solve the problem, the skilled person would not have turned to D7 or D17 for the solution according to claim 1 since, from the common general knowledge represented by D15 and D16, he would have expected that the features that distinguish claim 1 over the closest prior art D1 would have led to

a slower release of venlafaxine hydrochloride, and not a bioequivalent formulation as required.

- V. Opponents 1, 3 and 4 (appellant-opponents 1, 3 and 4) and the patent proprietor (appellant-patent proprietor) lodged appeals against that decision. With the letter of 29 October 2012, the appellant-patent proprietor submitted six sets of claims as first to sixth auxiliary requests.

The main request (claims as granted) and the second auxiliary request corresponded respectively to the main request and first auxiliary request underlying the appealed decision.

Claim 1 of auxiliary request 1 differed from claim 1 of the main request in that it indicated that the isolating/protecting/separating layer was "composed of polymers".

Claim 1 of auxiliary request 3 read as follows:

"1. An extended release composition comprising as active compound Venlafaxine Hydrochloride, which is obtainable by (a) coating Venlafaxine Hydrochloride on a non pareil inert core, (b) coating the coated core obtained in step (a) with an isolating/protecting/separating layer, and (c) coating the coated core obtained in step (b) with an additional polymeric layer controllably releasing the Venlafaxine Hydrochloride, wherein said composition comprises 0.5-10% of the isolating layer per weight of the total dosage form."

Claim 1 of auxiliary request 4 differed from claim 1 of the main request in that it specified that:

- a) the isolating/protecting/separating layer was composed of polymers selected from the group consisting of polyvinylpyrrolidone, hydroxypropylcellulose, hydroxypropylmethylcellulose, microcrystalline cellulose, carrageenan and GMS, and that
- b) the layer controllably releasing the Venlafaxine Hydrochloride was composed of a hydrophobic polymer selected from the group consisting of Eudragit and cellulose derivatives such as hydroxypropylmethylcellulose, ethyl cellulose or cellulose acetate mixed with a plasticizer selected from the group consisting of castor oil, dibutyl sebacate, glycerylmonostearate, diethylphthalate, glyceryl triheptanoate and triethyl citrate.

Claim 1 of auxiliary request 5 read as follows:

"1. An extended release composition comprising as active compound Venlafaxine Hydrochloride, in which Venlafaxine Hydrochloride is suitably connected to a binder selected from the group consisting of polyvinyl pyrrolidone, hydroxypropylcellulose and hydroxypropylmethylcellulose and coated on a non pareil inert core selected from an inert sugar core and a microcrystalline cellulose, which coated core is then coated with an isolating/protecting/separating layer composed of polymers selected from the group consisting of polyvinylpyrrolidone, hydroxypropylcellulose, hydroxypropylmethylcellulose, microcrystalline cellulose, carrageenan and GMS, which is then coated with an additional polymeric layer controllably releasing the Venlafaxine Hydrochloride which is composed of a hydrophobic polymer selected from the group consisting of Eudragit and cellulose derivatives

such as hydroxypropylmethylcellulose, ethyl cellulose or cellulose acetate mixed with a plasticizer selected from the group consisting of castor oil, dibutyl sebacate, glycerylmonostearate, diethylphthalate, glyceryl triheptanoate and triethyl citrate and wherein the composition comprises:

30-60% of said Venlafaxine Hydrochloride;
0.5-10% of said binder;
30-60% of said non pareil inert core;
0.5-10% of said isolating layer;
2-15% of said hydrophobic polymer; and
0.1-2% of said plasticizer,

in each case per weight of the total dosage form."

Claim 1 of auxiliary request 6 read as follows:

"1. An extended release composition comprising as active compound Venlafaxine Hydrochloride, in which Venlafaxine Hydrochloride is suitably connected to a polyvinyl pyrrolidone binder and coated on a non pareil inert sugar core, which coated core is then coated with an isolating/protecting/separating layer composed of polyvinylpyrrolidone, which is then coated with an additional polymeric layer controllably releasing the Venlafaxine Hydrochloride which is composed of ethyl cellulose mixed with a plasticizer selected from dibutyl sebacate, and wherein the composition comprises:

30-60% of said Venlafaxine Hydrochloride;
0.5-10% of said binder;
30-60% of said non pareil inert core;
0.5-10% of said isolating layer;
2-15% of said hydrophobic polymer; and

0.1-2% of said plasticizer,

in each case per weight of the total dosage form."

VI. With the grounds of appeal, the following evidence was submitted by appellant-opponent 4 and appellant-opponent 1 respectively:

D28: Declaration of John Kresevic dated 26 March 2012, and Exhibits 1, 2, 3 and 4 attached thereto

D29: Test report "Venlafaxine isolating layer comparative data".

VII. In a communication pursuant to Article 15(1) RPBA issued on 7 August 2015, the Board observed *inter alia* that the effect of bioequivalence (or of an equivalent dissolution profile) of the formulation of the invention to the formulation of D1 did not appear to be demonstrated by the evidence on file across the scope of claim 1 of all the requests.

VIII. In a letter dated 25 August 2015 opponent 2 (party as of right) informed the Board that it would not be attending the oral proceedings.

IX. By letter dated 25 August 2015, the appellant-proprietor submitted two further sets of claims as auxiliary requests 7 and 8.

Claim 1 of auxiliary request 7 corresponded to that of auxiliary request 6, with the following additional text:

".. where in said extended release composition has the following in vitro dissolution specifications in USP

apparatus 1 (basket) at 100rpm in purified water at 37°C:

<u>Time (hrs)</u>	<u>Average % venlafaxine HCL release</u>
<u>2</u>	<u><30</u>
<u>4</u>	<u>30-55</u>
<u>8</u>	<u>55-80</u>
<u>12</u>	<u>65-90</u>
<u>24</u>	<u>>80 "</u> .

X. Oral proceedings were held on 17 September 2015, during which the appellant-proprietor withdrew auxiliary request 8.

XI. As far as relevant for the present decision the arguments of the appellant-opponents can be summarised as follows:

a) Admittance of auxiliary requests 1 and 3 to 6

The scope of claim 1 of auxiliary request 1 was broader than that of claim 1 as maintained by the opposition division. This set of claims could have been filed during the first-instance proceedings. It was therefore not to be admitted into the appeal proceedings.

The subject-matter of auxiliary requests 3 to 6 differed from the subject-matter of the requests filed during the opposition proceedings. It was not the function of the appeal proceedings to assess the patentability of subject-matter not considered during the first-instance proceedings. Thus, these requests were not to be admitted either.

b) Inventive step - Main request and auxiliary requests 1 to 6

The closest prior art was represented by document D1. The formulation according to the patent in suit differed from the formulation of D1 mainly in that venlafaxine was coated on a non-pareil core and in the presence of an isolating/protecting/separating layer. The data disclosed in the experimental report D22, concerning the dissolution profile of a single composition, could not be extrapolated to a generic claim. Indeed, the drug release was controlled by various factors such as the amount of controlled release polymer, as demonstrated by Figure 4 of D7. It was therefore not credible that the technical problem of providing a venlafaxine composition having the same dissolution profile of the composition disclosed in D1 was solved across the whole scope of the claim. There were also no data showing particular effects associated with the presence of the separating layer. Hence, the technical problem was to provide a further sustained-release venlafaxine composition.

Document D7 disclosed sustained-release compositions comprising an inert core and the same sequence of layers as the compositions of the patent in suit. The compositions of D7 were suitable for a range of active ingredients, including highly water soluble drugs. The skilled person would have considered it obvious to prepare compositions as disclosed in D7 with the water soluble venlafaxine as active ingredient. The fact that the compositions could be prepared by a process requiring the use of a single apparatus did not support the presence of an inventive step, since the same process was disclosed in D7.

None of the prior-art documents indicated that venlafaxine was to be prepared only in dry conditions,

in order to prevent the formation of polymorphs. This could in principle also occur in a dry process. Moreover, the patent in suit was completely silent in relation to this issue.

The use of polyvinylpyrrolidone as polymer for the isolating layer was disclosed in example 3 of D14. Hence this feature did not render inventive the subject-matter of auxiliary request 6.

c) Admittance of auxiliary request 7

This request was filed at a very late stage of the proceedings. The features relating to the *in vitro* dissolution did not have a clear support in the original application. Auxiliary request 7 raised new issues, in particular in relation to the requirement of Article 123(2) EPC. This request could not be admitted.

XII. As far as relevant for the present decision, the arguments of the appellant-patent proprietor can be summarised as follows:

a) Admittance of auxiliary requests 1 and 3 to 6

These requests were admissible, since they had been filed with the reply to the appeals of the opponents and addressed the objections raised therein.

b) Inventive step - Main request and auxiliary requests 1 to 6

The compositions of the invention differed from the compositions disclosed in the prior-art document D1 in that venlafaxine was coated on an inert core and in the presence of a separating layer. The experiments

disclosed in D22 and D29 showed that claim 1 of the main request and auxiliary requests encompassed compositions having the same dissolution profile of the composition of D1. The claims also covered, however, compositions providing a different release of venlafaxine. The technical problem was the provision of a further extended release formulation comprising venlafaxine.

The contribution of the invention lay in the structure of the formulation and in the process for its preparation. In the composition of document D1, the active ingredient was mixed with excipients and then extruded-spheronised to form the core. During the process, venlafaxine was used in solid form and was never dissolved in a solvent. Both the composition and the process for its preparation were markedly different from the composition and the process of the patent in suit. In the compositions of the invention, the active ingredient was coated on the core. The skilled person would have avoided making important modifications to the structure of the formulation, since this could have had an impact on the dissolution profile of the drug. Furthermore, the skilled person had no reason to provide a formulation whose preparation required the dissolution of venlafaxine. Quite to the contrary, the information disclosed on page 4 of D1 that venlafaxine had two polymorphic forms would have discouraged the skilled person to dissolve the active ingredient in a solvent in order to avoid any possible transition from a crystalline form into a different one. An advantage offered by the compositions of the invention was represented by the fact that they could be prepared by a simplified process, requiring the use of a single apparatus.

As explained in D15 and D16, the purpose of the separating layer was to prevent the dissolution of the active ingredient into the external layer. This problem did not exist in the process of D1, since venlafaxine was not soluble in the organic solvents used therein. Thus, it was not required in the context of D1 to provide the formulation with a separating layer. In the composition of the patent, the separating layer was used to prevent an interaction between the active ingredient and the ethylcellulose of the extended release layer. Said use was entirely different from the one described in D15 and D16.

Claim 1 of auxiliary request 6 was restricted to compositions containing polyvinylpyrrolidone both as a binder and as a constituent of the separating layer. None of the prior-art documents suggested the use of this substance. Document D22 showed that a composition covered by claim 1 of auxiliary request 6 had the same dissolution profile of the composition of D1. It could not be excluded that the claim also encompassed compositions having a different dissolution profile.

c) Admittance of auxiliary request 7

Auxiliary request 7 was filed in response to the Board's communication of 7 August 2015. The subject-matter of this request was markedly restricted in order to address the concerns expressed by the Board as to whether the compositions covered by the claims had the same dissolution profile of the compositions of D1. The conditions for measuring the dissolution recited in claim 1 were disclosed in document D1.

XIII. The appellant-patent proprietor requested that the decision under appeal be set aside and the patent be

maintained on the basis of the claims as granted, or, alternatively, on the basis of auxiliary requests 1 to 6, filed with the letter of 29 October 2012, or auxiliary request 7, filed with the letter of 25 August 2015.

XIV. Appellant-opponents 1, 3 and 4 requested that the decision under appeal be set aside and the patent be revoked.

Reasons for the Decision

1. Main request (patent as granted) - Inventive step

The patent in suit addresses the problem of providing an alternative venlafaxine hydrochloride formulation, bioequivalent to that described in D1, via a more efficient method of preparation (paragraphs [0014] and [0032]).

1.1 Closest prior art

1.1.1 According to the decision under appeal, D1 represents the closest prior art. This view is shared by all the appealing parties, and the patent specification itself identifies D1 as the starting point for the skilled person. The Board sees no reason to deviate from this choice.

1.1.2 Document D1 concerns the provision of an improved encapsulated extended release dosage form of venlafaxine over that already known in the art (page 2, lines 36-37). Example 1 of D1 describes the preparation of an extended release capsule, whereby venlafaxine is blended with excipients in the presence of water, and

the resultant plastic mass of material is extruded, spheronised and dried to provide uncoated drug containing spheroids. A film coating is then added to the spheroids in a fluidised bed to obtain extended release film coated spheroids having a coating level of 3%. Spheroids having a specific particle size range are obtained by sieving and are subsequently filled into hard gelating capsules.

1.1.3 The extended release venlafaxine hydrochloride composition of claim 1 of the main request differs from the product of example 1 of D1 in that it comprises a non pareil inert core coated with venlafaxine hydrochloride and employs an isolating/protecting/separating layer between the venlafaxine hydrochloride layer and the controlled release polymeric coating. These differences were not disputed by the parties.

1.2 Technical problem

1.2.1 In order to define the objective technical problem underlying the subject-matter of claim 1, it must be investigated whether the alleged technical effects (of bioequivalence with the formulation of D1, and the provision of a more efficient method of preparation) associated with the distinguishing features are supported by the evidence on file. In this context, the term "bioequivalent" is understood to mean "having the same *in vitro* release pattern, or dissolution profile", since this is in fact what is measured according to all of the data on file: in the patent specification, the closest prior art D1, and the submitted test reports.

1.2.2 The patent specification does not provide evidence of bioequivalence, and the appellant-proprietor has relied solely on the data provided by test reports D22 and D29

as evidence that the effect is achievable across the entire scope of claim 1. D22 describes the preparation of an extended release composition according to claim 1, denoted sample A, and compares the dissolution profiles thereof with a composition according to D1 (Sample B). Although the exact composition of Sample B is not provided, the dissolution profiles of both samples are shown to fall within the ranges provided by the table in the specification (paragraph [0012]), which is an exact reproduction of that provided in D1 (page 5, lines 10-20). However, the fact that a specific composition such as sample A demonstrates the alleged effect is not evidence that the effect is achievable across the scope of the claim.

1.2.3 D29 on the other hand was filed by appellant-opponent 1 to demonstrate that the release profile of venlafaxine hydrochloride remained essentially identical despite variations in the thickness of the isolating/protecting/separating layer, which was in accordance with the teaching of D15. While the appellant-proprietor argues that the four compositions employed according to D22 and D29 were very different from each other and yet displayed an equivalent *in vitro* release pattern to that of the formulations of D1, it is apparent that at least as far as the controlled release polymer coating layer is concerned, very little variation is present. Consequently, the results of these tests cannot be generalised to any composition falling under the scope of claim 1.

1.2.4 In addition to the lack of relevant data provided by D22 or D29, the Board does not find it plausible that the release profile of the formulation of claim 1 is exclusively dependent on the particular layering system recited therein. In the expert declaration D28, Mr

Kresevic sets out the factors known to affect drug dissolution from controlled release polymeric drug formulations, and concludes that a wide range of drug dissolution profiles would be obtained when working within the scope of granted claim 1. In particular, in answer to question 1, a wide range of factors which were known to influence drug release were identified, only one of which concerned the quantity of controlled release coating applied. Indeed, focusing on this variable alone, it appears entirely logical that the amount, or thickness, of a *controllably releasing polymeric layer* will affect the dissolution profile of the active substance. This understanding is supported by *inter alia* the evidence provided by D7, wherein it is explicitly stated that during experiments it was observed that the thickness of functional coat (Surelease®, 25% w/w ethylcellulose) controlled the rate of drug release (page 13, lines 8-9 and Figures 3 and 4). This data is further corroborated by the disclosure of D16, which describes the preparation of non pareils layered with propranolol hydrochloride and sealed with a water-soluble polymer coating, followed by a Surelease® coating (table 6, page 253). In Figure 18 (page 253), the influence of the quantity of Surelease® applied on the release of the active drug was measured, and shows that the release profile of the drug in question (here: propranolol hydrochloride) varies depending on the thickness of the sustained release layer.

- 1.2.5 In view of these considerations, the Board concludes that the effect of bioequivalence is not achieved across the scope of claim 1. In this respect it is also observed that the appellant-patent proprietor, despite considering the formulations of the patent in suit as bioequivalent to the one of D1, also acknowledged that

the claims covered compositions having a different release profile.

1.2.6 In the Board's view, the alleged effect of providing a more efficient method of preparation than that of D1 is plausible, at least in view of the fact that a composition in accordance with claim 1 can be prepared starting from commercially available nonpareil cores via a stepwise application of the individual layers in a single type of equipment, which lies in contrast to the process to produce the composition of D1, which requires different equipment to blend, extrude, spheronise, dry, and coat the resultant spheroid and, as a consequence, more manipulation/intervention.

1.2.7 In view of these considerations, the Board holds that the objective technical problem is to provide a further extended release composition comprising venlafaxine hydrochloride as active agent, which can be prepared in a more efficient manner.

1.3 Obviousness

1.3.1 Document D7 relates to a process for the manufacture of sustained release beadlets containing a water soluble active agent. The process involves the application of a seal coat of a protective polymer to an inert sphere loaded with a drug. To the coated sphere obtained in this step, a further polymeric layer which regulates the drug release is applied (see page 6, lines 1 to 6 and page 9, lines 23 to 33). The whole process is carried out in a single apparatus, namely a fluid bed coater (page 9, lines 23 and 24). The product obtained by this process is a multi-layered beadlet which comprises, moving from the core to the outer layer, an inert core, a drug layer, a seal coating and a

sustained release polymeric coating (see figure on page 10). Since claim 1 of the patent in suit does not include any restriction as to the composition or structure of the isolating/protecting/separating layer, this cannot be distinguished from the seal coating of the beadlets of D7. Thus, the structure of the beadlets disclosed in D7, i.e. the sequence of layers, corresponds entirely to that of the extended release compositions of the patent in suit.

- 1.3.2 Hence, document D7 makes available a different technology from the one disclosed in D1 for the sustained release delivery of active ingredients, which is particularly suitable for water soluble drugs such as venlafaxin. Moreover, this technology offers the advantage that it can be carried out in a single apparatus.

By applying the technology of D7 to provide an extended release formulation of venlafaxine hydrochloride, the skilled person would easily arrive at the composition defined in claim 1 of the patent in suit.

- 1.3.3 In order to do this, the skilled person would simply need to follow the general instructions disclosed in the description of D7 or to replace in the procedures disclosed in the examples of D7 the active ingredient used therein with venlafaxine hydrochloride. Thus, the appellant patent-proprietor's argument that the skilled person would not consider to combine the teachings of D1 and D7, since these documents relate to very different processes requiring the use of different solvent systems, is not persuasive. A skilled person faced with the problem of providing an alternative formulation to the one disclosed in D1 would find in D7 a complete solution to this problem, i.e. the

description of such alternative formulation and the instructions for preparing it. He would therefore simply follow these instructions without any need to further consider the process of D1.

- 1.3.4 Contrary to the opinion expressed by the appellant patent-proprietor, the Board also considers that the existence of two polymorphic forms of venlafaxin hydrochloride would not discourage the skilled person from dissolving this drug in a solvent, as required by the process of D7.

The polymorphism of venlafaxin hydrochloride is briefly discussed on page 4 of D1 (lines 10 to 18). However, neither this document nor any other cited prior art indicates that a process involving the dissolution of venlafaxin hydrochloride in a solvent should be avoided in order to prevent the formation of polymorphic forms. The information that form I is the kinetic product of crystallization which can be converted to form II upon heating in the crystallization solvent (see D1, page 4, line 13) appears rather to suggest that the formation of a polymorphic mixture can easily be avoided.

There is therefore no objective basis which could support the existence of a sort of general prejudice against dissolving venlafaxine hydrochloride in a solvent.

- 1.3.5 The appellant-patent proprietor also argued that the separating layer of the composition of the patent in suit had the purpose of preventing an interaction between the active ingredient and the polymer of the extended release layer. In the formulations disclosed in the prior-art document, the separating layer had a

different purpose, namely to prevent the dissolution of the active ingredient into the external layer.

In this respect, the Board observes that there is no evidence to support the allegation that the separating layer in the formulations of the patent in suit may provide some particular technical effect, different from the technical effects provided, for instance, by the seal coating in the compositions of D7. In any case, as already remarked above, claim 1 does not include any restriction as to the composition or structure of the isolating/protecting/separating layer, which is therefore not distinguishable from the seal layer of D7. Thus, the fact that the isolating/protecting/separating layer is introduced in the formulation with a specific purpose merely expresses a mental act which cannot contribute to the inventiveness of the claim even if this purpose is not mentioned in D7.

1.4 For the above reasons, the subject-matter of claim 1 of the main request does not fulfil the requirements of Article 56 EPC 1973.

2. Admittance of auxiliary requests 1 to 6

2.1 These requests were submitted by the appellant-patent proprietor on 29 October 2012 for the first time in reply to the statements of grounds of appeal of the appellant-opponents.

Auxiliary request 2 is identical to that upheld by the opposition division and its admittance was not challenged.

2.2 The appellant-opponent 3 expressed the view that auxiliary request 1 should have been filed during the first-instance proceedings, since claim 1 is broader than claim 1 of the patent maintained in amended form by the opposition division. The appellant-patent proprietor argued that its requests were filed in direct response to the appellant-opponents' objections raised against the patent as granted in the statements of grounds of appeal.

The Board observes in this respect that the patent proprietor has appealed the decision of the opposition division. It is therefore in principle entitled to file requests of a broader scope than the request which formed the basis for the decision by the first-instance department to maintain the patent in amended form. When such requests are not filed with the grounds of appeal but at a later stage, they do not form the basis of the patent proprietor's appeal under Article 12(1)(a) RPBA and their admittance would usually be assessed according to the provisions of Article 13 RPBA. However, when, as in the present case, the opponent(s) also filed an appeal against the first-instance decision and the broader request is filed in reply to the appeal(s) of the opponent(s), the patent proprietor is acting as a respondent and its request is presented under Article 12(1)(b) RPBA. Thus the provisions of Article 12(4) RPBA apply with regard to the question whether a request filed with this reply is admitted into the appeal proceedings.

According to Article 12(4) RPBA, without prejudice to the power of the Board "to hold inadmissible facts, evidence or requests which could have been presented ... in the first instance proceedings", everything presented by the parties under Article 12(1)

RPBA has to be taken into account by the Board if and to the extent it relates to the case under appeal and meets the requirements in Article 12(2) RPBA.

- 2.3 In the Board's view, the appellant-patent proprietor could have been expected to present the present auxiliary request 1 in the first-instance proceedings under the circumstances of the present case. However, claim 1 of auxiliary request 1 differs only very slightly from claim 1 of the main request (see point V above). It is furthermore easy to understand the difference, and no additional complexity has been added to the discussion in appeal proceedings.

Thus, exercising its discretion under Article 12(4) RPBA, the Board admitted auxiliary request 1 into the appeal proceedings.

- 2.4 The subject-matter of the claims of auxiliary requests 3 to 6 is narrower in scope than that of the claims of the patent maintained in amended form by the opposition division. They were filed with the reply to the appeals of the appellant-opponents and therefore form the basis of the appeal proceedings according to Article 12(1)(b) RPBA.

In the Board's view there are no reasons for considering that the appellant-patent proprietor should have filed these requests during the first-instance proceedings, since the patent was maintained in amended form on the basis of broader claims. Consequently, the Board took into account auxiliary requests 3-6 in the appeal proceedings under Article 12(4) RPBA.

3. Auxiliary request 1 - Inventive step

3.1 Claim 1 of this request differs from claim 1 of the main request in that it indicates that the isolating/protecting/separating layer is composed of polymers.

3.2 The appellant-patent proprietor did not submit any new argument to support the inventive merit of the claimed subject-matter of this request.

The Board notes that the seal coating of D7 is also composed of polymers (see for instance page 9, lines 25 to 27). Hence, the considerations set out in respect to the main request also apply to the subject-matter of claim 1 of auxiliary request 1.

It follows that the subject-matter of claim 1 of auxiliary request 1 does not fulfil the requirements of Article 56 EPC 1973.

4. Auxiliary request 2 - Inventive step

4.1 Claim 1 of auxiliary request 2 differs from the corresponding claim of the main request in that it specifies that the amount of isolating/protecting/separating layer represents from 0.5 to 10% of the weight of the dosage form.

4.2 No arguments were submitted by the appellant-patent proprietor in respect of the inventive merit of the claimed subject-matter of this request.

4.3 Since claim 1 does not contain any limitation as to the polymeric layer controlling the release of venlafaxin or the chemical composition of the isolating/protecting/separating layer, the considerations set out

in point 1.2 above also apply here, with the consequence that the objective technical problem over D1 is still to be formulated as the provision of a further extended release composition comprising venlafaxine hydrochloride as active agent, which can be prepared in a more efficient manner.

- 4.4 The amount of seal coating in the compositions of D7 can vary from 0 to 20% and is preferably between 2 and 5% (page 21, lines 29 to 31). Thus, the limitation introduced in claim 1 of this request does not render the teaching of D7 less relevant.

It follows that the conclusions presented above as to the obviousness of the subject-matter of claim 1 of the main request also apply to the subject-matter of claim 1 of auxiliary request 2. Hence, the claimed subject-matter of this request does not fulfil the requirement of inventive step.

5. Auxiliary request 3 - Inventive step

- 5.1 Claim 1 of this request is worded as a product-by-process claim. The formulation defined in this claim is not different from that of auxiliary request 2, as also stated by the appellant patent-proprietor in its submissions of 29 October 2012.

Thus, the claimed subject-matter of this request does not fulfil the requirement of inventive step for the reasons submitted in respect of auxiliary request 2.

6. Auxiliary request 4 - Inventive step

- 6.1 Claim 1 of this request differs from claim 1 as granted in that it indicates which polymers can be used for the

isolating/protecting/separating layer and which polymers and plasticizers can be included in the layer controlling the vanlafaxine hydrochloride release (see point V above).

- 6.2 Despite these limitations, both layers may still have a highly variable composition. This appears particularly true for the extending release layer, whose composition depends on the selection of a hydrophobic polymer and a plasticiser. Thus, in the Board's opinion the experimental results disclosed in D22 and D29 cannot be generalized to the whole scope of claim 1 of this request.

Indeed, the appellant-patent proprietor did not submit any specific argument in relation to this request, but simply referred to the submissions set out in respect of the main request.

Accordingly, the Board considers that the technical problem is the same as that formulated in respect of the main request.

- 6.3 At least some of the products listed in claim 1 as possible components of the isolating/protecting/separating layer and controlled-release layer are also mentioned in D7 for the same applications. Thus, hydroxypropylmethylcellulose, useful as material for the isolating/protecting/separating layer, is also mentioned on page 10 of D7 (lines 20 to 23) as one of the preferred polymers for the seal coating. The preferred material for the sustained release layer of the formulation of D7 is Surelease® (page 13, line 8 to page 14, line 9), which is a product containing ethylcellulose and a plasticizer such as dibutyl sebacate (see document D15, table 14). Ethylcellulose

and dibutyl sebacate are both recited in claim 1 of auxiliary request 4 as components of the controlled-release layer (respectively as hydrophobic polymer and as plasticiser).

Thus, the teaching of D7 also maintains its relevance in respect of the claimed subject-matter of auxiliary request 4. It follows that the considerations set out in respect of the main request are applicable here too.

The subject-matter of claim 1 of auxiliary request 4 is therefore not inventive.

7. Auxiliary request 5 - Inventive step

7.1 Compared with claim 1 of auxiliary request 4, claim 1 of this request further requires the presence of a binder. It also specifies that the inert core must be selected from a sugar core and microcrystalline cellulose. Moreover, the claim provides the relative amounts of the components of the formulation (see point V above).

7.2 The observations made in 6.2 above as to the high variability of the composition of the layers also apply to the formulations covered by this request. Thus, the technical problem is the same as formulated in respect of the main request.

7.3 The limitations introduced in claim 1 are based on features which can be derived from the teaching of D7. For instance, on page 26 of this document (lines 9 to 17) it is disclosed that polyvinyl pyrrolidone and hydroxypropylmethylcellulose can be used as binders, and on page 10 (lines 12 to 17) it is affirmed that the inert core can be made of sugar or microcrystalline

cellulose. These same materials are recited in claim 1 of auxiliary request 5 for the same use.

As to the percentages defining the relative amounts of the components, it is noted that these are not linked to any particular effect. In such situations, setting suitable ranges is regarded as a routine activity which does not require any inventive skill. Moreover, the Board observes that in example 1 of D7 the percentages of the various components fall in the ranges defined in claim 1 of auxiliary request 5.

7.4 Thus, the reasoning set out in respect of the main request also applies here. Hence, the subject-matter of claim 1 of auxiliary request 5 does not meet the requirements of Article 56 EPC 1973.

8. Auxiliary request 6 - Inventive step

8.1 Claim 1 of auxiliary request 6 specifies the substance used as binder, the composition of the inert core, the polymer used for the isolating/protecting/layer and the composition of the controlled release layer (see point V above).

8.2 Also in respect of this request, the appellant-patent proprietor defined the technical problem as the provision of a further extended release formulation comprising venlafaxine. Questioned by the Board during the oral proceedings as to whether the subject-matter of claim 1 was substantially limited to compositions providing the same release profile of the compositions of D1, the appellant-patent proprietor affirmed that the claim might still also include compositions having a different release profile.

In this respect, the appellant-opponents underlined that the range defining the amount of ethyl cellulose, i.e. the controlled release polymer, was still very broad, i.e. between 2 and 15%. It was therefore not credible that the compositions encompassed by the claim had the same release profile.

- 8.3 As discussed in point 1.2.4 above, D7 and D16 show that the amount of controlled release polymer has a marked impact on the dissolution profile of the active ingredient. This finding was confirmed by Mr Kresevic in his declaration (D28). In view of this consideration, and taking into account the common position expressed by the parties during the oral proceedings (see point 8.2 above), the Board concludes that in this case too, the effect of bioequivalence with the formulations of D1 is not achieved across the scope of claim 1.

Thus, the technical problem is to be formulated again as the provision of a further extended release composition comprising venlafaxine hydrochloride as active agent, which can be prepared in a more efficient manner.

- 8.4 The appellant-patent proprietor argued that in the composition of claim 1 both the binder and the polymer of the isolating/protecting/separating layer were made of polyvinyl pyrrolidone, and that this characteristic was not suggested in the prior art.

The Board observes that D7 also suggests using polyvinyl pyrrolidone as binder (page 26, line 16). As to the polymer for the isolating/protecting/separating layer, D7 does not provide any particular restriction. However, the use of polyvinyl pyrrolidone as separating

layer is known from D14 (column 4, lines 31 to 45 and example 3). Thus, the choice of this material as a component of the isolating/protecting/separating layer cannot render the composition inventive in the absence of any particular effect associated with this choice.

- 8.5 The materials used for the other components of the formulation, namely sugar for the inert core and a mixture of ethyl cellulose with dibutyl sebacate for the polymer controllably releasing the active ingredient, are also disclosed in D7 (see points 6.3 and 7.3 above). Thus, the selection of these materials does not provide any inventive contribution to the subject-matter of claim 1 either.

It follows that the subject-matter of claim 1 of auxiliary request 6 does not meet the requirements of Article 56 EPC 1973.

9. Auxiliary request 7 - Admittance

- 9.1 According to Article 13(1) RPBA, the Board has discretion in deciding whether to admit any amendment to a party's case after its filing of the grounds of appeal or its reply. The discretion shall be exercised in view of *inter alia* the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy.
- 9.2 The sole claim of auxiliary request 7 was filed by the appellant-patent proprietor with its letter of 25 August 2015, i.e. less than one month before the date of the oral proceedings. Hence, this claim constitutes an amendment to the appellant-patent proprietor's case within the meaning of Article 13(1)

RPBA and consequently may be admitted at the board's discretion.

The appellant-patent proprietor explained that this request was filed in response to the observations made by the Board in its communication of 7 August 2015, in relation to the question as to whether it was rendered credible by the evidence on file that the compositions of the patent in suit had the same dissolution profile as the composition of D1.

- 9.3 The Board notes that this issue was raised by appellant-opponents 3 and 4 in their statements setting out the grounds of appeal (see paragraphs 26 and 8.4.1 respectively) and by appellant-opponent 1 in its submissions of 17 May 2013 (paragraph 1.2.2). Moreover, it is clear from the appealed decision (see point 6.9) that the opponents had already questioned the possibility of generalising the experimental data of D22 to the whole scope of the claim in the first-instance proceedings.

Accordingly, the appellant-patent proprietor could have addressed the issue concerning the breadth of the claim in relation to available experimental evidence well before receiving the Board's communication.

- 9.4 Independently of the above considerations, it appears that the new features recited in claim 1 concerning the conditions at which the dissolution of venlafaxine is determined are not clearly and unambiguously disclosed in the original application.

The appellant-patent proprietor explained that these features were disclosed on page 5, lines 8 and 9 of document D1. However, although the application as filed

refers to document D1, it does not contain any reference to this specific passage of D1. Hence, it is at least doubtful whether the amendments introduced in claim 1 of auxiliary request 7 comply with the requirements of Article 123(2) EPC.

9.5 Consequently, the Board, exercising its discretion under Article 13(1) RPBA, decided not to admit the late-filed auxiliary request 7 into the appeal proceeding, since it raises new issues, which goes against the requirement of procedural economy.

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:



S. Fabiani

J. Riolo

Decision electronically authenticated