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Datasheet for the decision of 20 September 2013

Case Number: T 0418/09 - 3.3.07

Application Number: 00971346.2

Publication Number: 1223914

IPC: A61K9/00, A61K31/55

Language of the proceedings: EN

Title of invention:
ORALLY DISINTEGRATING COMPOSITION COMPRISING MIRTAZAPINE

Patent Proprietor:
MSD Oss B.V.

Opponents:
ETHYPHARM
Teva Pharmaceutical Industries, Ltd.
Tecnimede

Headword:
Orally disintegrating composition comprising mirtazapine/MSD OSS

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no)

Decisions cited:

Catchword:

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Case Number: T 0418/09 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 20 September 2013

Appellant: (Patent Proprietor)	MSD Oss B.V. Kloosterstraat 6 5349 AB Oss (NL)
Representative:	Buchan, Gavin MacNicol Merck & Co., Inc. European Patent Department Hertford Road Hoddesdon, Hertfordshire EN11 9BU (GB)
Respondent: (Opponent 1)	ETHYPHARM 21, rue Saint-Matthieu B.P. 45 78550 HOUDAN (FR)
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Respondent: (Opponent 2)	Teva Pharmaceutical Industries, Ltd. Har Hotzvim 91010 Jerusalem (IL)
Representative:	von Uexküll - Güldenband, Alexa Vossius & Partner Siebertstrasse 4 81675 München (DE)
Representative:	
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 5 December 2008 revoking European patent No. 1223914 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman:	J. Riolo
Members:	D. Boulois
	P. Schmitz

Summary of Facts and Submissions

I. European patent No. 1 223 914 based on application No. 00 971 346.2 was granted on the basis of a set of 5 claims. The sole independent claim read as follows:

"1. A dosage unit for peroral administration, comprising a pharmaceutical formulation of mirtazapine or a pharmaceutically acceptable salt thereof as an active substance, pharmaceutically acceptable excipients, and a layer, which is coating mirtazapine and which substantially prevents mirtazapine from being released orally, wherein the dosage unit is of the orally-disintegrating type, and the layer disintegrates in an acidic environment."

II. Three oppositions were filed against the granted patent. The patent was opposed under Article 100(a) and (b) EPC, on the grounds that its subject-matter lacked novelty and inventive step and was not sufficiently disclosed.

III. The documents cited during the opposition and appeal proceedings included the following:
(1) EP 0 436 252
(4) US 5 464 632
(9) Physician Desk Reference, 1998, 52nd edition, pp 1956-1959, p. 2346
(26) Bruna et al., 1998, Proc. Intl. Symposium Control. Rel. Bioact. Mater. 25, pp 938-939
(27) Di Constanzo, 9.10.2007/10.10.2007, 7th International GLATT Symposium/Marseille
(28) Journal Officiel du 20.12.1998, Avis d'octroi d'autorisations de mise sur le marché de spécialités pharmaceutiques, p. 3

(38) Actualités Pharmaceutiques, Septembre 1999, 49-50,"La technologie Flashtab® au service du paracétamol"
(39) www.pharmaceuticalonline.com, "Prographarm to market Flashtab technology in the US", 5 August 1999
(40) www.drugdiscoveryonline.com, "Prographarm launches Flash Tab in Italy", 9 August 9, 1999
(47) Int. J. of Psychiatry in Clinical Practice, 2009, 1-8, "Treating depression with different galenic drug formulations: Does it make a difference? The comparison of mirtazapine fast dissolving formulation (FDT) with conventional mirtazapine tablets (CT)".

IV. The present appeal lies from the decision of the opposition division to revoke the patent. The decision was based on 2 sets of claims, namely claims 1-5 of the patent as granted as main request, and claims 1-3 of the auxiliary request filed during the oral proceedings of 17 November 2008.

V. In the decision under appeal, the opposition division considered the subject-matter of claim 1 of the main request to be novel over documents (9) and (1), since none of the documents disclosed an orally disintegrating dosage unit, and the former did not disclose a coating around the active agent mirtazapine.
As regards inventive step, document (9) was seen as an appropriate starting point, and the problem to be solved was to provide taste-masked mirtazapine formulations which were bioequivalent with tablet formulations and which had an improved ease of administration.
The technical effects provided by the present invention were directly and unambiguously derivable from the teaching of any of documents (4), (26), (27) and (28),

leading to the lack of inventive step of claim 1 of the main request.

It was also considered that, since the orally disintegrating mirtazapine dosage units were obvious and provided predictable and desirable technical effects, any further technical effect, such as the reduction of the side effects, in particular on weight gain, could only be considered as a bonus effect.

The subject-matter of claim 1 of auxiliary request 1 differed from claim 1 of the main request by the addition of the feature characterising the coating layer, namely "*a layer made of Eudragit E100, which layer...*".

The opposition division considered that the use of the trademark "*Eudragit E100*" led to a lack of clarity of the claim, because the meaning of such a term might change during the lifetime of a patent and because the term denoted a particular polymer in a particular granule form that could not be seen as a clear definition for the coating. Thus, the auxiliary request did not meet the requirements of Article 84 EPC.

VI. The patent proprietor filed an appeal against said decision.

With the notice of appeal the appellant submitted 3 sets of claims as main request, second and third auxiliary requests, the first auxiliary request being the set of claims as granted. With the statement of grounds of appeal new pieces of evidence were filed.

VII. Respondents 01 and 02, respectively opponents 01 and 02, submitted arguments and new pieces of evidence in reply to the appeal.

VIII. With a letter dated 31 January 2013, the appellant submitted a main request and auxiliary requests 1-9.

The main request corresponded to the set of claims as granted.

The subject-matter of the independent claims of the auxiliary requests read as follows, difference(s) compared with the main request shown in bold:

a) Auxiliary request 1

The subject-matter of claim 1 of auxiliary request 1 was the same as the subject-matter of claim 1 of the main request.

b) Auxiliary request 2

"1. A dosage unit for peroral administration, comprising a pharmaceutical formulation of mirtazapine or a pharmaceutically acceptable salt thereof as an active substance, pharmaceutically acceptable excipients, and a layer, which is coating mirtazapine and which substantially prevents mirtazapine from being released orally, wherein the dosage unit is of the orally-disintegrating type, **and the layer is a butylmethacrylate-(2-dimethylaminoethyl) methacrylat-methylmethacrylat-copolymer(1:2:1) with average molecular weight of approximately 150,000.**"

c) Auxiliary request 3

The subject-matter of claim 1 of auxiliary request 3 differed from the subject-matter of claim 1 of auxiliary request 2 by the further addition of the

feature **"and the mirtazapine on its turn is coated onto inert particles".**

d) Auxiliary request 4

The subject-matter of claim 1 of auxiliary request 4 was the same as the subject-matter of claim 1 of the main request.

e) Auxiliary request 5

"1. A dosage unit for peroral administration, comprising a pharmaceutical formulation of mirtazapine or a pharmaceutically acceptable salt thereof as an active substance, pharmaceutically acceptable excipients, and a layer, which is coating mirtazapine and which substantially prevents mirtazapine from being released orally, wherein the dosage unit is of the orally-disintegrating type, **and the layer is Eudragit® E100 ("Butylmethacrylate-(2-dimethylaminoethyl) methacrylat-methylmethacrylat-copolymer(1:2:1)")."**

f) Auxiliary request 6

The subject-matter of claim 1 of auxiliary request 6 differed from the subject-matter of claim 1 of auxiliary request 5 by the addition of the feature **"and the mirtazapine on its turn is coated onto inert particles".**

g) Auxiliary request 7

"1. A dosage unit for peroral administration, comprising a pharmaceutical formulation of mirtazapine or a pharmaceutically acceptable salt thereof as an active substance, pharmaceutically acceptable

excipients, and a **polymer** layer, which is coating mirtazapine and which substantially prevents mirtazapine from being released orally, wherein the dosage unit is of the orally-disintegrating type, and the layer disintegrates in an acidic environment **and the mirtazapine on its turn is coated onto inert particles**".

h) Auxiliary request 8

The subject-matter of claim 1 of auxiliary request 8 differed from the subject-matter of claim 1 of auxiliary request 7 by the addition of the feature "and the mirtazapine on its turn is coated **onto inert non-pareils**".

i) Auxiliary request 9

The subject-matter of claim 1 of auxiliary request 9 differs from the subject-matter of claim 1 of the main request, by the introduction of the feature **"and wherein the dosage unit has the same strength, and is bioequivalent with, a conventional tablet containing 30 mg of mirtazapine**".

IX. With a letter dated 15 July 2013, respondent 03 withdrew its opposition.

X. A Board's communication dated 6 August 2013 was sent to the parties.
It drew in particular the attention of the parties to important points relating to the assessment of inventive step. It raised *inter alia* some points already mentioned by the respondents, namely whether or not it could have been expected that a dosage unit as claimed might reach the same bio-equivalence as a

dosage unit such as the commercial product Remeron®, and whether an effect on weight gain had indeed been achieved, and whether this effect might be considered as a "bonus effect" or not.

XI. With a letter dated 6 September 2013, respondent 01 informed the board and the parties that it would not be represented at the oral proceedings.

XII. Oral proceedings took place on 20 September 2013.

XIII. The arguments of the appellant, as far as relevant to the present decision, may be summarised as follows:
Document (9) was seen as the closest prior art.
The differences between the subject-matter of claim 1 of the main request and the teaching of document (9) were the orally disintegrating type dosage unit and the presence of a coating layer surrounding mirtazapine and disintegrating in an acidic environment. Several effects resulted from these differences, namely an earlier onset of action of the antidepressant, an improved patient compliance, a reduction of the side effects, as shown by documents (21) and (47), and bio-equivalence with the conventional tablet, as shown by document (25).
The problem could thus be seen as the provision of a dosage unit offering bio-equivalence with the conventional tablets, an improved compliance, and a diminution of the side effects, in particular less weight gain.
The provision of an orally disintegrating form could not be seen as an easy task, particularly for an antidepressant drug such a mirtazapine, as an orally disintegrating form for such class of drugs did not exist yet.

The achievement of bio-equivalence was shown by document (25) and constituted a surprise, because of the different solubility and release profile of the tablets. The conventional rapid release tablet released mirtazapine in the mouth and the gastrointestinal tract, while the orally disintegrating form did not release the drug in the mouth but progressively in the gastrointestinal tract, starting the release in the stomach after dissolution of the coating surrounding the mirtazapine. These different solubility and release profiles of the tablets would not have led the skilled person to expect bio-equivalence.
Document (27) showed that the design of an orally disintegrating form such as the Flash-Tab® form necessitated four successive design steps and a fair amount of development time, namely at least 18 months, without a guarantee of feasibility or success. Document (27) did not disclose that the orally disintegrating tablets had a coating around the drug, even less an acid-sensitive coating. Moreover, there was no indication in this document that the Flash-Tab® purpose was to achieve a rapid release form.
Starting from document (9) the skilled person had thus no guidance to the preparation of the claimed dosage units.
Document (40) did not provide further information, especially regarding bio-equivalence, and amounted only to an invitation to start a research program.

As regarded the decreased weight gain observed with the claimed dosage unit, documents (21) and (47) showed clearly the existence of such an effect. The technical effect was plausible and credible, and based on a plausible pharmacological mechanism, linked with the absence of stimulation of the 5-HT_2 and 5-HT_3 receptors in the stomach by the orally disintegrating form. This

effect was of particular importance, given the long-term administration of the drug, and the deleterious effect of increased weight on the depressed patients. This effect could thus not be considered as a bonus effect.

As regards the subject-matter of claim 1 of auxiliary request 3, the modification added a structural non obvious feature, since no prior art taught that the active should be coated on inert particles, and such particles processed into an orally disintegrating tablet. This structural difference was thus not obvious.
The same argumentation was valid as regards the specification of the type of polymer in the auxiliary requests.

XIV. The arguments of respondent 02, as well as those submitted in writing by respondent 01, as far as relevant to the present decision, may be summarised as follows:

It was obvious to make a bio-equivalent generic form of the existing conventional tablet.
Some technological platforms, such as the Flash-Tab® platform, were available at the priority date for making orally disintegrating tablets. The aim of these platforms was to render the generic form available, to switch from the rapid release tablet to the orally disintegrating tablet. It could thus not be surprising to achieve the bio-equivalence.
The absorption of a drug coated with a polymer dissolving in an acidic environment was similar to a conventional rapid release tablet, since the solubility of the drug and the site of absorption of the drug did not vary from one form to another. The skilled person

would have expected that two forms releasing the drug at the same site would be bio-equivalent.
Document (27) showed how easy it was to prepare such a bio-equivalent formulation, since all the steps followed in the design procedure constituted routine steps. Since the site of release of mirtazapine from the conventional tablet was known, as was its pharmacokinetics, it was easy to prepare a bio-equivalent tablet, thanks to the Flash-Tab® technology presented in document (27). The various technical alternatives of the Flash-Tab® technology were presented in detail by document (4), particularly in its examples.

As regards the side effects, especially the reduced weight gain observed with the orally disintegrating form of mirtazapine, the evidence, namely documents (21) and (47), was submitted in the form of meta-analysis and not in the form of a direct comparison. Thus, the effect was not credibly shown. Moreover, the existence of such an improvement was contradictory to the bio-equivalence stated to be observed between the conventional form and the orally disintegrating form. It was also questionable if the observed difference in weight gain of 0.3 kg could be considered as significant. It merely corresponded to a daily individual weight variation.
It was also not possible to rely on the study performed on another antidepressant drug, to explain the diminution of weight gain, namely olanzapine, since the dosage units were different, in particular with an absence of coating over olanzapine in the orally disintegratable form. This effect was thus seen as an artefact which could not be checked since the data were not available.

XV. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or auxiliary requests 1 to 9 filed with letter dated 31 January 2013.

XVI. Respondent 02 requested that the appeal be dismissed. The same was requested in writing by respondent 01.

Reasons for the Decision

1. The appeal is admissible

2. Main request- Inventive step

2.1 The invention relates to a dosage unit for peroral administration of mirtazapine, which can fully serve as a substitute for the marketed tablets Remeron® (see paragraphs [0001], [0005], [0006]). The dosage unit has the same strength and is bio-equivalent with the conventional tablets and can be used to bring about improved effects of mirtazapine and diminished side effects (see paragraphs [0003], [0007]).

2.2 Document (9) relates to the commercial reference product of mirtazapine, namely Remeron®, and discloses its composition and characteristics of use (see page 1956, central column). It mentions that Remeron® is a film-coated tablet for peroral administration, which is rapidly and completely absorbed following oral administration and has a peak plasma concentration within about two hours after oral administration (see page 1956, right col.).
This document shows that the commercial tablet Remeron® is a tablet to be swallowed and not of the orally

disintegrating type, and that it does not comprise a coating around mirtazapine which disintegrates in an acidic environment.

The choice of this document as the closest prior art was not contested.

2.3 The problem as set out in the description of the present invention may be seen as the provision of a dosage form which brings improvements to the administration of mirtazapine, and which has the same strength and is bio-equivalent to the conventional tablets (see paragraph [0005]]).
The improvements concern some of the beneficial effects of mirtazapine, such as better sleep, a stronger anxiolytic effect, and an earlier onset of antidepressant activity, as well as an improved patient compliance. Another improvement relates to the diminution of side effects, in particular of weight gain (see paragraphs [0003] and [0007]).

2.4 As a solution to this alleged problem, claim 1 of the main request proposes a dosage unit for peroral administration comprising a formulation of mirtazapine, with in particular a coating layer surrounding the mirtazapine, the said coating preventing mirtazapine from being released orally and disintegrating in an acidic environment, and the dosage unit being of the orally disintegrating type.

2.5 It has to be investigated whether there is sufficient evidence supporting the alleged effects.

2.5.1 The patent in suit provides three examples, one being a bio-equivalence test in example 2. A comparison is made between an orally disintegrating tablet according to

the formulation of example 1 and the marketed tablet Remeron®.

Example 2 concludes that the test formulation and the reference formulation are bio-equivalent with respect to the maximum concentration C_{max} and the areas under the curve AUC_{0-dast} and $AUC_{0\rightarrow\infty}$. These experimental results on these parameters are supported by the numbered results given in Table 1, which show a bio-equivalence for the C_{max} and the two AUC within the required 90% confidence interval.

Example 2 and Table 1 thus demonstrate convincingly the bio-equivalence between the claimed dosage unit and the commercial tablet Remeron®.

Example 3 deals with a test on the onset of antidepressant activity, as well as body weight, sexual functioning and other effects associated with mirtazapine. Apart the statement that the subjects are assessed to find antidepressant activity within the first and second week of treatment, the example does not give any comparison with the effects obtained with the commercial tablet Remeron®, even less any result or data regarding the mentioned effects.

Thus, the examples of the description succeed in showing the bio-equivalence of the claimed dosage units with the commercial tablets. This is further confirmed by the teaching of document (25) which reproduces the tests of example 2.

However, none of the examples shows any results or data regarding the improvements of some of the beneficial effects of mirtazapine or the diminution of the side effects.

2.5.2 Document (47) has been submitted by the appellant to demonstrate the existence of an improved effect, in

particular the diminution of a specific side effect, namely weight gain.
The document reported the results of an *a posteriori* analysis of pooled data of 25 trials with conventional tablets of mirtazapine and of 5 trials with a fast disintegrating tablet of mirtazapine according to the present invention. The aim of this analysis was to examine the weight changes assessed in these studies. The fast-disintegrating tablet of mirtazapine was associated with an average of 0.3 kg less weight gain up to 6 weeks of treatment (see "Weight changes", page 6: Figure 1). No significant difference in weight gain was stated for the two first weeks and up to 8 weeks of treatment.
The same *a posteriori* analysis of 25 trials with conventional tablets of mirtazapine and of 5 trials with a fast disintegrating tablet of mirtazapine reported by document (21) confirmed this tendency, with a calculated difference in weight gain of an average 0.5 kg up to 6 weeks of treatment.

These results are relativized by the authors of the studies themselves, who recognise the limitations of the study, since it was not based on strictly comparative studies and it did not consider the psycho-pathological profiles of the patients in which weight increased and those in which it did not, and the effect of different dosing schedules in the studies (see document (47), page 5, right column, or document (21), page 3, "Conclusions").
The study of document (47) is indeed a meta-analysis showing only a slight difference in weight gain between the two types of dosage units, in particular when one considers individual daily weight variations. This difference in weight increase is even statistically not significant in the two first weeks and after 8 weeks of

treatment, for which no explanation could be provided in document (47).

This absence of statistical significance for the weight increase in the two first weeks and after 8 weeks of treatment combined with the the weak difference of weight increase up to 6 weeks and with the limitations of the study casts a doubt on the relevance of the results.

The content of document (30) casts additional doubts on the validity of the study. Figure 1 of this document shows a direct comparison between 2 studies with an orally disintegrating form of mirtazapine and 10 studies with the conventional tablet of mirtazapine. It proves that one of the two studies with the fast-disintegrating tablet of mirtazapine has a weight increase greater than most of the studies performed with the conventional tablets.

The appellant gave an explanation regarding the possible mechanism responsible for a difference in the weight increase, based on the the affinity of mirtazapine for the gastrointestinal receptors 5-HT_2 and 5-HT_3 (see document (47), page 5, 2nd paragraph of right column, 2nd paragraph of left column). This explanation was supported by a study comparing an orally disintegrating tablet and a conventional formulation of olanzapine, another antidepressant drug, and showed an effect on weight increase linked with a more rapid gastrointestinal transit of the orally disintegrating tablet of olanzapine. This rapid transit involved thus a shorter duration of interaction with the receptors 5-HT_2 and 5-HT_3, and a significant reduction of weight increase.

This explanation cannot however convince the board in the absence of any information regarding the structure of the dosage forms of olanzapine and their corresponding pharmacokinetic behaviour. Moreover, the proven bio-equivalence between the orally disintegrating form and the conventional tablet of mirtazapine tends to show that the gastrointestinal transit is similar for both forms. The explanation given by the appellant is thus not convincing.

Consequently, in the absence of any experimental evidence or arguments establishing a minimum plausibility, the presence of an improvement to the administration of mirtazapine in terms of the beneficial or the side effects of mirtazapine has not been credibly demonstrated.

2.5.3 As a consequence, the only beneficial effect of the claimed subject-matter demonstrated over the prior art is the achievement of bio-equivalence and the improvement of the patient's compliance.

The problem underlying the present invention is thus seen as the provision of a dosage form which has the same strength as and is bio-equivalent with the conventional tablets and which improves the compliance of the patients.

2.6 Document (40) relates to the Flash-Tab® oral drug formulation from "Laboratoires Prographarm", which offers a platform technology for quick-dissolving tablets. According to document (40) the Flash Tab® technology can be tailor-made to any pharmacokinetic profiles such as rapid release, as shown by the figures of document (40).

The teaching of document (40) has been evaluated at the priority date of the present patent, and is confirmed by several other documents, namely document (27) (see pages 2-4), document (38) (see first page) or document (39), which all show that there is no reason to doubt the teaching of document (40).

The Flash-Tab® technology is technically disclosed in detail in the corresponding patent document (4) from "Laboratoires Prographarm" which shows the preparation of orally rapidly disintegrating tablets based on coated microgranules of the drug. The nature of the excipients and of the coating is adapted to the release to be achieved (see col. 23, l. 40-45) and the orally disintegrating nature of the tablet eases its administration and the patient's compliance (see col. 2, l. 40-57). Example 2 of document (4) thus shows a composition with a structure similar to the preferred composition of the present invention, namely a fast-disintegrating oral dosage tablet comprising the drug coated with a polymer dissolving in an acidic environment, namely Eudragit® E.

Consequently, the provision of an orally disintegrating tablet with an active substance coated with a layer disintegrating in an acidic environment and presenting bio-equivalence with an existing tablet is a solution known to the skilled person, and can be prepared without undue burden or difficulty. The provision of such a dosage unit is a common and obvious solution to the posed problem.

2.7 Further argument from the appellant

According to the appellant, it was not predictable that an orally disintegrating dose unit could achieve bio-

equivalence with a conventional rapid release tablet, in view of the different sites of absorption of the forms, namely the gastrointestinal tract for the former and first the mouth and then the gastrointestinal tract for the latter, and it was also a surprising solution since no orally disintegrating forms existed for antidepressant drugs.

Moreover, it relied on the contents of document (27) to question the ease and the feasibility of the preparation of the Flash-Tab® formulations, in view of the multiple steps and the 18 months design procedure from the feasibility step to submission to the health authorities (see document (27), pages 7-8).

The board cannot follow these arguments.

The pharmacokinetic profile and the structure of the conventional coated tablet Remeron® was known from document (9). The said tablet had to be swallowed and the pharmacokinetics corresponded to a rapid-release tablet with the gastrointestinal tract as site of absorption. A release from the swallowed film-coated tablet and the further absorption of mirtazapine in the mouth is not credible in view of these facts.

As to the duration of 18 months of a development project, this timespan is usual and normal in the pharmaceutical field and was to be expected in order to perform all the routine experimentation. It does not constitute an excessive or undue burden.

As regards the nature of the active agent, the description of document (4) mentions that the technology can be adapted to any drug, including antidepressant drugs (see col. 2, l. 25).

2.8 Consequently, the main request does not meet the requirements of Article 56 EPC.

3. Auxiliary request 1 - Inventive step

Since the subject-matter of claim 1 of auxiliary request 1 is identical to claim 1 of the main request, the same conclusion applies *mutatis mutandis*, and it does not meet the requirements of Article 56 EPC.

4. Auxiliary request 2 - Inventive step

The subject-matter of claim 1 of auxiliary request 2 differs from the main request by the specification of the polymer which forms the coating over the active substance, namely "*a butylmethacrylate-(2-dimethylaminoethyl) methacrylat-methylmethacrylat-copolymer(1:2:1) with average molecular weight of approximately 150,000*".
Since example 2 of document (4) discloses the same polymer, the reasoning for inventive step used for the main request and its further conclusion apply *mutatis mutandis* to claim 1 of auxiliary request 2. No inventive step can be seen as a result of the further addition of this technical feature.
Auxiliary request 2 does not meet the requirements of Article 56 EPC.

5. Auxiliary request 3 - Inventive step

The subject-matter of claim 1 of auxiliary request 3 differs from claim 1 of auxiliary request 2 in the specification of the way that mirtazapine is processed, namely *"and the mirtazapine on its turn is coated onto inert particles"*.
Since this specific processing is not associated with any particular technical effect and is also disclosed in example 5 of document (4), it has no effect on the conclusions reached previously for auxiliary request 2.

Auxiliary request 3 therefore does not meet the requirements of Article 56 EPC.

6. Auxiliary request 4 - Inventive step

Since the subject-matter of claim 1 of auxiliary request 4 is identical to claim 1 of the main request, the same conclusion applies, and it does not meet the requirements of Article 56 EPC.

7. Auxiliary request 5 - Inventive step

The subject-matter of claim 1 of auxiliary request 5 differs from claim 1 of the main request by the specification of the polymer which forms the coating over the active substance, namely "*Eudragit® E100 ("Butylmethacrylate-(2-dimethylaminoethyl) methacrylat-methylmethacrylat-copolymer(1:2:1)")*". Since this polymer is also disclosed in example 2 of document (4), this modification has no effect on the argumentation and conclusions on inventive step reached previously for the main request.

Auxiliary request 5 does not meet the requirements of Article 56 EPC.

8. Auxiliary request 6 - Inventive step

The subject-matter of claim 1 of auxiliary request 6 differs from the subject-matter of claim 1 of auxiliary request 5 by the further addition of the feature *"and the mirtazapine on its turn is coated onto inert particles"*, which was also known from document (4) (see example 5).

No inventive step can be seen as a result of the further addition of this technical feature, like for auxiliary request 3.

Auxiliary request 6 does not meet the requirements of Article 56 EPC.

9. Auxiliary request 7 - Inventive step

The subject-matter of claim 1 of auxiliary request 7 differs from the main request by the specification of the nature of the coating, namely "*a polymer layer*", and that "*the mirtazapine on its turn is coated onto inert particles*".
Document (4) discloses the use of a polymer as coating and the coating of the active agent on neutral sugar spheres, also called non-pareils. No particular effect and inventive step can be seen as a result of the further addition of these technical features.
The subject-matter of claim 1 of auxiliary request 7 is obvious, and auxiliary request 7 does not meet the requirements of Article 56 EPC.

10. Auxiliary request 8 - Inventive step

The subject-matter of claim 1 of auxiliary request 8 differs from auxiliary request 7 in the specification of the inert particle, namely that "*the mirtazapine on its turn is coated onto inert non-pareils*".
This modification has no effect on the argumentation and conclusions reached previously for auxiliary request 7.
Auxiliary request 8 does not meet the requirements of Article 56 EPC.

11. Auxiliary request 9 - Inventive step

The subject-matter of claim of auxiliary request 9 differs from the main request by the introduction of the feature *"and wherein the dosage unit has the same*

strength, and is bioequivalent with, a conventional tablet containing 30 mg of mirtazapine".

This feature merely expresses the desirable result to be achieved, and cannot contribute to the inventive step of the claim.

Auxiliary request 9 does not meet the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

S. Fabiani J. Riolo

Decision electronically authenticated