Internal distribution code:

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

Datasheet for the decision of 12 April 2016

Case Number: T 0382/13 - 3.3.07

Application Number: 08717753.1

Publication Number: 2120884

IPC: A61K9/20

Language of the proceedings: EN

Title of invention:
Pharmaceutical composition

Patent Proprietor:
Boehringer Ingelheim International GmbH

Opponent:
Zentiva k.s.

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - main and auxiliary requests (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 0382/13 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 12 April 2016

Appellant: (Opponent)	Zentiva k.s. U kabelovny 130 10237 Praha 10 (CZ)
Representative:	Plougmann Vingtoft a/s Rued Langgaards Vej 8 2300 Copenhagen S (DK)
Respondent: (Patent Proprietor)	Boehringer Ingelheim International GmbH Binger Strasse 173 55216 Ingelheim am Rhein (DE)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 20 December 2012 rejecting the opposition filed against European patent No. 2120884 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	J. Riolo
Members:	A. Usuelli
	P. Schmitz

Summary of Facts and Submissions

I. European patent EP 2 120 884, based on European patent application No. 08717753.1, was granted on the basis of twelve claims.

Claim 1 as granted read as follows:

"1. A pharmaceutical tablet or tablet layer comprising the angiotensin II receptor antagonist telmisartan in amorphous form, a basic agent and sorbitol, characterized in that the sorbitol has a specific surface area of between 0.75-3.5 m^2/g, preferably 1.4-3.0 m2/g and most preferred 2.0-2.5 m^2/g."

II. 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. The following documents were among those cited during the first-instance proceedings:

D1: WO 03/059327
D2: US 6,274,778
D3: US 4,507,511
D4: US 4,252,794
D8: Pharmaceutical Technology, 8(9), 42-53, (1984)

III. By decision posted on 20 December 2012, the opposition division rejected the opposition.

According to the decision under appeal:

(a) The requirement of sufficiency of disclosure was met.

(b) The tablet or tablet layer defined in claim 1 of the patent in suit was novel over the disclosure of example 2 of D1 on account of the requirement that sorbitol had a specific surface area between 0.75 and 3.5 m^2/g.

(c) Document D1 was the closest prior art for the assessment of inventive step. The technical problem was defined as the provision of tablets having at the same time improved hardness, higher dissolution rates and improved reproducibility. Documents D2, D3 and D4 were not concerned with the problem of improving the dissolution rate and reproducibility. Document D8 did not suggest any link between surface area and hardness. Hence, the skilled person would not have combined the teaching of D1 with the teaching of D2 to D4 or D8 to arrive at the solution proposed in the patent in suit. The requirements of Article 56 EPC were therefore met.

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

V. By a letter dated 16 September 2013 the patent proprietor (respondent) responded to the appeal and submitted two auxiliary requests.

Claim 1 of auxiliary request 1 was identical to claim 1 of the patent as granted.

Claim 1 of auxiliary request 2 differed from claim 1 as granted in the addition of the following feature at the end of the claim:

"wherein the tablet or tablet layer comprises 3 to 50% by weight of telmisartan; 0.25 to 20% by weight of basic agent; and 3 to 95% by weight of sorbitol."

VI. Oral proceedings were held on 12 April 2016.

VII. With regard to the requirement of inventive step, the appellant essentially argued as follows in respect of all requests:

The closest prior art was the composition disclosed in example 2 of document D1. The formulation defined in claim 1 of the patent differed from the composition of document D1 on account of the specific surface area of sorbitol. The experimental data reported in the patent were not sufficient to demonstrate any improvement over the closest prior art. In particular, the tests disclosed in examples 6 and 9 for determining the dissolution rate were always carried out with tablets containing sorbitol with a specific surface area of 2 m^2/g. However, according to claim 1, the specific surface area of sorbitol could vary over a broad range. There was no reason to generalise the results of examples 6 and 9 to any tablet included in claim 1. Furthermore, it followed from paragraph [0007] of the patent that the telmisartan tablets did not need to dissolve very rapidly. There was also no evidence of an improved reproducibility of the dissolution and hardness parameters. Indeed, the formulations used for the comparative tests contained sorbitol with a variable specific surface area. In contrast thereto, the sorbitol used for the formulations according to the patent had a specific surface area. This difference rendered meaningless any consideration concerning the reproducibility of the results. Documents D2 to D4 and D8 indicated that it was possible to obtain tablets

with improved hardness by the use of sorbitol having a specific surface area as defined in claim 1 of the patent. Accordingly, the skilled person would have considered it obvious to prepare telmisartan tablets containing sorbitol having a specific surface area in the range 0.75-3.5 m^2/g.

VIII. The arguments of the respondent in relation to the requirement of inventive step of all the requests can be summarised as follows:

The tablets of the patent in suit differed from the telmisartan tablet disclosed in example 2 of D1 on account of the specific surface area. The experimental data disclosed in the patent showed that it was possible to improve the hardness of the tablets using a sorbitol of high specific surface area. Moreover, examples 6 and 9 showed that the dissolution rate of the tablets was not impaired, despite the increase in hardness. The experiments of examples 6 and 9 were of particular relevance since the tablets tested were the hardest tablets disclosed in the patent. The experimental data demonstrated also a significant improvement of the reproducibility of dissolution and hardness parameters. The fact that the tablets of the invention maintained a good dissolution rate despite the increase in hardness was not to be expected since, as discussed in document D8, hard tablets usually suffered from a slow dissolution rate. None of the prior-art documents suggested using a sorbitol material with a specific surface area as defined in claim 1 for preparing telmisartan tablets. Document D2 did not relate to formulations concerning telmisartan. Moreover, it disclosed tablets to be sucked which did not need to dissolve as rapidly as the tablets of the patent in suit. Similar considerations applied to the

tablets disclosed in D3. The problem addressed in these documents was simply to provide hard tablets. The dissolution profile of the formulations was not an issue. Thus, the skilled person trying to improve the hardness of the tablet of D1 while maintaining the same dissolution properties would not have considered the teaching of these prior art documents.

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

X. The respondent requested that the appeal be dismissed. Alternatively, that the decision under appeal be set aside and that the patent be maintained on the basis of auxiliary requests 1 or 2 filed on 16 September 2013.

Reasons for the Decision

Main request - granted patent

1. Inventive step

The invention underlying the patent in suit relates to a pharmaceutical tablet or tablet layer comprising as active ingredient telmisartan, a product developed for the treatment of hypertension (see[0001] and [0002] of the patent specification).

1.1 Closest prior art

1.1.1 According to the decision under appeal, document D1 represents the closest prior art. This view is shared by the parties, and the Board sees no reason to differ.

1.1.2 Example 2 of D1 relates to a tablet containing in two different layers the active ingredients telmisartan and

hydrochlorthiazide. The telmisartan layer comprises in addition to the active ingredient also a basic agent, namely sodium hydroxide, and sorbitol. The description of D1 explains that telmisartan is contained in the formulation in substantially amorphous form.

Thus, the telmisartan layer disclosed in example 2 of D1 presents all the features of the formulation defined in claim 1 of the patent in suit, with the exception of the specific surface area of the sorbitol, in respect of which no information is given in D1. Accordingly, the subject-matter of claim 1 differs from the disclosure of D1 on account of the requirement that it contains sorbitol with a specific surface area of between 0.75 and 3.5 m^2/g.

1.2 Technical problem

1.2.1 According to the description, the problem addressed by the inventors was to provide telmisartan tablets (or tablet layers) "displaying dissolution rates and hardness levels being both at most preferable levels" ([0012]). Furthermore, the tablets should present an improved reproducibility of dissolution and hardness parameters ([0015]).

1.2.2 Examples 5 to 11 of the patent disclose experiments in which telmisartan tablets according to claim 1 are compared with tablets having the same composition but containing sorbitol of a specific surface area, between 0.5 and 0.7 m^2/g.

Examples 5, 7, 8, 10 and 11 report the results of experiments in which the hardness of the tablets has been determined. The tablets according to claim 1 tested in these examples contain sorbitol with a

specific surface area of 1.3 m^2/g, 1.4 m^2/g, 1.8 m^2/g and 2 m^2/g. In all the examples, these tablets are harder than the comparative tablets in which sorbitol has a specific surface area between 0.5 and 0.7 m^2/g. These data confirm the teaching that can be derived from table III of D8 (page 48), namely that the hardness of a sorbitol-containing tablet increases when the specific surface area of the sorbitol increases.

In the light of these data, the Board accepts that the use of sorbitol with a specific surface area in the range 0.75-3.5 m^2/g provides tablets of high hardness.

1.2.3 Experiments for determining the dissolution rate of the tablets are disclosed in examples 6 and 9 of the patent. The tests of example 6 relate to a tablet according to the patent in suit comprising sorbitol with specific surface area of 2 m^2/g and a comparative tablet of identical composition containing sorbitol with a specific surface area in the range 0.5-0.7 m^2/g. The dissolution mean value for the composition according to claim 1 is slightly higher than the value determined for the comparative composition (91 vs. 87).

Example 9 differs from example 6 in that the formulation representing the patent in suit is a telmisartan layer which is part of a bilayer tablet containing also a hydrochlorothiazide layer. As for the tablet of example 6, the telmisartan layer contains sorbitol with a specific surface area of 2 m^2/g. The dissolution mean value of the telmisartan layer is slightly below the value of the comparative composition (97 vs. 98).

1.2.4 In the respondent's opinion, the results of examples 6 and 9 show that the tablets according to the patent in

suit maintain a good dissolution rate despite the high value of hardness. This result was surprising since, as indicated in document D8 (page 53, left column, second full paragraph), hard tablets have a slow rate of dissolution.

1.2.5 The Board agrees that the tablets according to claim 1 tested in examples 6 and 9 have substantially the same dissolution rate as the comparative tablets. However, the data concerning the dissolution rate of the tablets according to claim 1 relate to two formulations both containing sorbitol with a specific surface area of 2 m^2/g (see point 1.2.3 above). In contrast, claim 1 covers a range of telmisartan tablets in which the specific surface area of sorbitol can vary from 0.75 to 3.5 m^2/g.

The experimental data disclosed in the patent in relation to the hardness of the tablets indicate that this parameter is strongly influenced by the value of the specific surface area of sorbitol. For instance, in example 5 an increase in the sorbitol specific surface area from 0.5-0.7 m^2/g to 2 m^2/g results in a variation of the hardness from 107 N to 204 N. It follows from this that the hardness of the telmisartan tablets covered by claim 1 can be highly variable in view of the broad range of the sorbitol specific surface area recited in claim 1.

1.2.6 As explained above, the respondent's central argument was based on the assumption that it was part of common general knowledge that increasing the hardness of a tablet would impair the dissolution rate. In the Board's view, if this assumption is accepted, there must be an adequate level of evidence showing that in the present case, unexpectedly, the dissolution rate is

not linked to the hardness. In other words, the results of single experiments carried out using samples having similar or identical characteristics (in the present case the same specific surface area) cannot be easily generalised also to other samples with different characteristics when these results diverge from what a skilled person would normally expect.

1.2.7 It follows from the above considerations (see point 1.2.5) that the hardness of tablets comprising sorbitol of a specific surface area close to the end points of the range of claim 1 may be very different from that of the tablet layers tested in examples 6 and 9. In particular, a telmisartan tablet comprising sorbitol of a specific surface area close to the upper limit of 3.5 m^2/g is likely to be much harder than a tablet containing sorbitol of a specific surface area of 2 m^2/g.

In the absence of experimental data confirming the results of examples 6 and 9 also for tablets containing sorbitol of a higher specific surface area, it cannot be established whether the unexpected dissolution behaviour shown in these examples is retained over the whole scope of the claim or whether, depending on the value of the specific surface area of sorbitol, the generally accepted rule that hard tablets dissolve slowly prevails.

Accordingly, in the Board's opinion the evidence available in relation to the dissolution rate of the tablets does not allow any conclusion to be drawn that is of general validity over the whole scope of claim 1.

1.2.8 According to paragraph [0015] of the description, the formulations of the patent are also characterised by an

improved reproducibility of the dissolution and hardness parameters.

As observed by the appellant, in each example of the description the comparative formulations contain sorbitol with a specific surface area defined by a range, namely 0.5 to 0.7 m^2/g. In contrast, the formulations according to the patent contain sorbitol with a specific (i.e. single) value of specific surface area. Thus, the sorbitol used for the preparation of the comparative formulations appears to be less homogeneous, in terms of specific surface area, than the sorbitol used for the formulations of the patent in suit. No arguments were submitted by the respondent about this. Under these circumstances the Board considers that no comparison can be made of the reproducibility of the dissolution and hardness parameters.

1.2.9 In the light of the above considerations, the technical problem can be formulated as the provision of tablets or tablet layers of high hardness containing telmisartan as active ingredient and sorbitol.

1.3 Obviousness

1.3.1 The question to be answered in relation to the obviousness of the solution is whether the skilled person would solve the technical problem defined above by the provision of telmisartan tablets according to example 2 of D1, in which the sorbitol used has a specific surface area in the range 0.75 to 3.5 m^2/g.

1.3.2 Documents D2 to D4 and D8 disclose modified sorbitol materials having specific surface areas within the range defined in claim 1 of the patent in suit.

Document D2 states that the high compressibility of the sorbitol disclosed therein has a positive effect on the mechanical strength of the tablets (column 4, lines 6 to 14). The specific surface area of this sorbitol is at least equal to 2 m^2/g (claim 1). It is furthermore affirmed that the tablets manufactured with this sorbitol exhibit high compressibility, i.e. high hardness for a low relative density (column 10, lines 18 to 23).

Document D3 discloses a modified sorbitol with improved tableting properties having a specific surface area of 0.7 to 1.5 m^2/g (claim 1). The paragraph bridging columns 3 and 4 of this document states that "with the same compressive force, very much harder tablets can be obtained with the sorbitol according to the invention".

Document D4 relates to a new type of sorbitol having a specific surface area of at least 1 m^2/g (claim 1). This sorbitol is used in the preparation of tablets of improved hardness (column 3, lines 16 to 22 and example 1).

In document D8, the properties of a variety of crystalline sorbitol products are discussed. The experimental results reported in Table III (page 49) indicate that three samples of sorbitol of a specific surface area between 1.05 m^2/g and 1.51 m^2/g provide tablets which are harder than sorbitol samples having a specific surface area of 0.60 m^2/g or below.

1.3.3 From the above discussion, it clearly emerges that sorbitol products of a specific surface area within the range defined in claim 1 can be advantageously used to prepare tablets of high hardness. Hence, the skilled

person trying to maximise the hardness of the telmisartan tablet of D1 would use one of the sorbitol materials of high surface area described in D2 to D4 and D8, thereby arriving at the subject-matter of claim 1.

1.3.4 The respondent argued that documents D2 to D4 related mainly to tablets for sucking, a pharmaceutical form which was not suitable for the administration of telmisartan.

Documents D2 (example 6) and D3 (column 4, line 3) do indeed refer to the preparation of tablets for sucking as an advantageous way of using the sorbitol products. However, neither these documents nor documents D4 or D8 restrict the use of the sorbitol materials disclosed therein to the preparation of a specific type of tablets. Hence, the skilled person concerned with the preparation of telmisartan tablets would have no reason to disregard the teaching of these documents in relation to the use of sorbitol of high specific surface area for preparing tablets of high hardness.

1.3.5 The Board agrees with the respondent that in documents D2 to D4 and D8 the problem of maintaining a good dissolution rate of the tablets is not considered.

However, as discussed above (see points 1.2.3 to 1.2.7), in the Board's view there is no convincing evidence in the present case that the problem of maintaining a good dissolution rate has been solved over the whole scope of the claim.

Additionally, the Board observes that according to paragraph [0007] of the description the telmisartan tablets are considered to have a satisfying dissolution

rate if at least 75% of the active ingredient is dissolved after 30 minutes. As pointed out by the appellant, this information indicates that the tablets of the patent in suit do not need to have a particularly high dissolution rate.

Under these circumstances, the Board considers that the skilled person would not disregard *a priori* the teaching of D2 to D4 and D8, afraid that an increase in the hardness would compromise the dissolution rate of the tablets. He would very likely use a sorbitol of high specific surface area in order to achieve a good level of hardness and then verify whether the dissolution rate of the tablets is still acceptable.

1.4 In view of the foregoing, the Board concludes that the subject-matter of claim 1 of the patent as granted is not inventive.

Auxiliary request 1

2. Claim 1 of auxiliary request 1 is identical to claim 1 of the patent as granted. Consequently, auxiliary request 1 likewise fails to fulfil the requirements of Article 56 EPC.

Auxiliary request 2

3. The limitations introduced in claim 1 of this request as to the amounts of telmisartan, basic agent and sorbitol do not result in any new distinguishing feature over the disclosure of D2. Furthermore, since the specific surface area of sorbitol is defined as in claim 1 of the patent, the considerations set out in points 1.2.3 to 1.2.7 above in relation to the

dissolution rate of the tablets apply also to claim 1 of auxiliary request 2.

It follows that also auxiliary request 2 does not involve an inventive step.

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