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Datasheet for the decision of 4 September 2020

Case Number: T 0746/18 - 3.3.07

Application Number: 12007638.5

Publication Number: 2730279

IPC: A61K9/16, A61K9/20, A61K31/137

Language of the proceedings: EN

Title of invention:
Immediate release formulations of cinacalcet

Patent Proprietor:
K.H.S. Pharma Holding GmbH

Opponent:
Gillard, Richard Edward

Headword:
Cinacalcet formulations / K.H.S. PHARMA HOLDING GMBH

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no)

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Case Number: T 0746/18 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 4 September 2020

Appellant: (Opponent)	Gillard, Richard Edward Elkington and Fife LLP Thavies Inn House 3-4 Holborn Circus London EC1N 2HA (GB)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Respondent: (Patent Proprietor)	K.H.S. Pharma Holding GmbH Rheinstraße 49 55218 Ingelheim am Rhein (DE)
Representative:	Bendele, Tanja RUHR-IP Patentanwälte Brucker Holt 58 45133 Essen (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 10 January 2018 concerning maintenance of the European Patent No. 2730279 in amended form.**

Composition of the Board:

Chairman	A. Usuelli
Members:	E. Duval
	P. Schmitz

Summary of Facts and Submissions

I. European patent 2730279 (hereinafter "the patent") was granted on the basis of 13 claims. Claim 1 of the patent as granted read as follows:

"Pharmaceutical composition, comprising:
(a) from 15 to 50% by weight cinacalcet HCl;
(b) from 30 to 80% by weight of one or more fillers;
(c) from 5.1% to 7% by weight of one or more binders;
and optionally one or more disintegrants, one or more glidants and/or one or more lubricants or one or more other acceptable pharmaceutical excipients, wherein the percentage by weight is relative to the total weight of the composition."

II. An opposition was filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, and it was not sufficiently disclosed.

III. The opposition division took the interlocutory decision that, on the basis of auxiliary request 2, the patent met the requirements of the EPC.

The decision was based on the patent as granted as main request, on auxiliary request 1 filed during the oral proceedings before the opposition division, and on auxiliary request 2 with claims filed with the letter dated 1 September 2017 and a description adapted thereto.

IV. Claim 1 of auxiliary request 2 read as follows:

"Pharmaceutical composition, comprising:

(a) from 15 to 50% by weight cinacalcet HCl, wherein the cinacalcet HCl particles exhibits a D_{50} ranging from 10 µm to 30 µm;
(b) from 30 to 80% by weight of one or more fillers, wherein said fillers are selected form starch, microcrystalline cellulose, dicalcium phosphate lactose, calcium carbonate, magnesium carbonate, sorbitol, mannitol, sucrose, dextrin, kaolin, magnesium oxide, calcium sulfate, xyitol, isomalt, glucose, fructose, maltose, citric acid, tartaric acid, fumaric acid, copolymers from vinyl pyrrolidone and vinyl acetate or co-polymers of polyethylene glycol, and mixtures thereof,
(c) from 5.5% to 7% by weight of a binder, wherein said binder is povidone,
and optionally one or more disintegrants, one or more glidants and/or one or more lubricants or one or more other acceptable pharmaceutical excipients, wherein the percentage by weight is relative to the total weight of the composition."

V. The decision cited among others the following documents:

D1: WO2005034928
D7: Pharmaceutics: The Science of Dosage Form Design, Second Edition, Ed. M.E. Aulton, 2002, pages 404-408
D16: Pharmaceutics: The Science of Dosage Form Design, Second Edition, Ed. M.E. Aulton, 2002, pages 397-412
D20: Anlage 1 (experimental data) filed by letter dated 1 September 2017

VI. The opposition division decided in particular the following:

(a) As a result of the overlap of the filler and binder components, claim 1 of the main request did not meet the requirements of sufficiency of disclosure.

(b) The subject-matter of auxiliary request 1 lacked novelty over D1.

(c) Auxiliary request 2 was admitted into the proceedings. It met the requirements of Articles 123(2), 123(3), 83 and 84 EPC, and its subject-matter was novel.

D1 represented the closest prior art. The subject-matter of claim 1 of auxiliary request 2 differed from the disclosure of D1 in that:
1. the cinacalcet HCl particles exhibited a D_{50} ranging from 10 µm to 30 µm, and
2. the amount of povidone binder was from 5.5% to 7% by weight.
The technical effect of the claimed particle size was a low solubility of cinacalcet HCl, whereas the effect of the claimed amount of povidone was an improved solubility of cinacalcet HCl particles having D_{50} ranging from 10 µm to 30 µm.
The objective technical problem was the provision of a pharmaceutical formulation, which had a rapid release profile of cinacalcet HCl exhibiting a small particle D_{50} over a broad range of active drug load. The claimed solution was not rendered obvious by the prior art.

VII. The opponent (appellant) appealed the above decision of the opposition division. In its statement setting out the grounds of appeal, the appellant cited the following document D21, and contested among others that auxiliary request 2 involved an inventive step.

D21: The Handbook of Pharmaceutical Excipients, Sixth Edition, Eds. R.C. Rowe et al., The Pharmaceutical Press London, 2009, pages 208-210 and 663-666.

VIII. By letter dated 13 September 2018, the patent proprietor (respondent) indicated that it had no interest in the maintenance of the patent. The respondent made no request nor replied in substance to the appeal.

IX. The Board notified on 15 June 2020 its preliminary opinion regarding in particular inventive step, and set a time limit of 2 months for the parties to reply. No reply was received.

X. The arguments of the appellant, in as far as relevant to the present decision, may be summarised as follows:

(a) D1 represented the closest prior art. It disclosed (see paragraph [0057]) a tablet comprising cinacalcet HCl, fillers and binders. The distinguishing feature of claim 1 of auxiliary request 2 was the amount of the specific binder.

The skilled person would expect small particle sizes to equate with rapid dissolution. In contrast, figure 4 of the patent showed a reduction of dissolution rate at low particle size. In light of D16, this behaviour could rather be explained by cohesion and aggregation of fine particles, which could be addressed by proper formulation. D20 did not provide appropriate comparative results and could not demonstrate an effect of the amount of binder. The technical problem was the provision of an alternative formulation.

The claimed solution was obvious. D1 stated that the cinacalcet particles should have a D_{50} at or below 50 µm. The textbook D7 indicated that binders were typically included in formulations at 2-10% by weight. Accordingly, the criteria of Article 56 EPC were not fulfilled.

XI. The appellant requests that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

1. Inventive step, auxiliary request 2 (Request allowed by the opposition division)

1.1 D1 is selected as closest prior art in the appealed decision and by the appellant. The Board sees no reason to differ.

D1 discloses (see claims 78 and 87; paragraph [0033]; example at paragraph [0057]) a pharmaceutical composition comprising:
- 10-40% cinacalcet HCl having a D_{50} less than or equal to 50µm,
- 45-85% of a diluent such as starch or cellulose, and
- 1-5% binder such as povidone (see paragraphs [0033], [0038], [0039] and the example).

1.2 Regarding the differentiating features, the Board agrees with the reasoning of the opposition division. The subject-matter of claim 1 of auxiliary request 2 differs in that:
- the cinacalcet HCl particles exhibit a D_{50} ranging from 10 µm to 30 µm, and

- the amount of povidone binder is 5.5-7% by weight.

1.3 However, the Board shares the appellant's view that no technical effect has been shown to arise as a result of these differences.

1.3.1 With respect to the claimed D_{50} range of 10-30 µm and the alleged associated lower solubility of cinacalcet HCl, the decision relies on paragraph [0015], table 2 and figure 4 of the patent. However, these data compare a composition as claimed, comprising cinacalcet HCl particle having D_{50}=20µm, with compositions where D_{50}=89 or 82µm, i.e. the comparison is not made with the D_{50} values of up to 50µm considered in the closest prior art D1 but with values lying well above. Hence no effect is shown to arise from the selection of the claimed D_{50} range.

1.3.2 As to the higher amount of povidone, the appealed decision refers to D20 as evidence of an effect on the dissolution rate. In D20, a comparative composition x is described and its dissolution profile is compared to a "Patent formulation" whose composition is unknown. If, as indicated in the appealed decision, this patent formulation corresponds to example 2 of the patent, then it differs from the comparative composition x not only in respect of the amount of povidone but also in respect of several other features, including the disintegrant and the fillers.

Whereas example 2 comprises a total of 11% sodium starch glycolate as disintegrant, the disintegrant in comparative composition x consists in 6% crospovidone. The opposition division reasoned that comparative composition x exhibits a slower dissolution rate than the patent formulation despite having a higher ratio of

disintegrant to binder. This reasoning ignores the fact that the nature of the disintegrants, and their mechanism of action, are different. As shown in D21 (see section 7 for both entries), sodium starch glycolate causes disintegration by a rapid uptake of water followed by rapid and enormous swelling. In contrast, crospovidone is a water-insoluble tablet disintegrant which has high capillary activity which leads to tablet disintegration with little tendency to form gels.

In view of the above, the Board cannot share the opposition division's opinion that the further differences between example 2 and comparative composition x are minor. As a result, no conclusion can be drawn as to the effect of the higher amount of povidone binder alone.

1.4 The Board therefore agrees with the appellant that the objective technical problem is the provision of an alternative formulation.

D1 already discloses that the cinacalcet HCl particles should exhibit a D_{50} less than or equal to 50 µm. The selection of the range 10-30 µm, without any associated effect, does not involve an inventive step. Furthermore, the general disclosure of D1 does not require the amount of binder to be in the range of 1-5 % by weight. The skilled person would therefore consider using typical amounts of binder, such as the 2-10% by weight indicated in the textbook D7. The claimed amounts of 5.5-7% by weight are entirely encompassed within these typical amounts.

Accordingly, auxiliary request 2 does not fulfill the criteria of Article 56 EPC.

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:

A. Nielsen-Hannerup A. Usuelli

Decision electronically authenticated