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Datasheet for the decision of 28 September 2020

Case Number: T 2584/18 - 3.3.07

Application Number: 14166756.8

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Language of the proceedings: EN

Title of invention:
Controlled Release 25-Hydroxyvitamin D

Applicant:
Opko Ireland Global Holdings, Ltd.
Opko Renal, LLC

Headword:
Controlled Release 25-Hydroxyvitamin D/Opko Ireland Global Holdings, Ltd, Opko Renal, LLC

Relevant legal provisions:
EPC Art. 83

Keyword:
Sufficiency of disclosure - (no)

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Case Number: T 2584/18 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 28 September 2020

Appellant: (Applicant 1)	Opko Ireland Global Holdings, Ltd. Citywest Business Campus 3013 Lake Drive Dublin 24 (IE)
Appellant: (Applicant 2)	Opko Renal, LLC 4400 Biscayne Boulevard Miami, FL 33137 (US)
Representative:	Barker Brettell LLP 100 Hagley Road Edgbaston Birmingham B16 8QQ (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 29 May 2018 refusing European patent application No. 14166756.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	D. Boulois
	Y. Podbielski

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse European patent application n° 14 166 756.8, published as EP 2 762 132 A1, which is a divisional application of the application EP 08 746 908.6.

II. The decision was based on the sets of claims filed as main request with letter of 31 January 2017 and as auxiliary requests 1-3 with letter of 1 December 2017.

Claim 1 of the main request read as follows:

"1. 25-hydroxyvitamin D for use in the treatment of hyperparathyroidism, wherein the 25-hydroxyvitamin D is administered by intravenous delivery via controlled release."

Claim 1 of the auxiliary requests 1 to 3 read as follows, the difference with respect to the main request being indicated in **bold**:

Auxiliary request 1

"1. 25-hydroxyvitamin D for use in the treatment of hyperparathyroidism, wherein the 25-hydroxyvitamin D is administered by intravenous delivery via controlled release, **and wherein the 25-hydroxyvitamin D is administered in dosage amounts of from 1 to 100 µg per day.**"

Auxiliary request 2

"1. 25-hydroxyvitamin D for use in the treatment of hyperparathyroidism, wherein the 25-hydroxyvitamin D is administered by intravenous delivery via controlled release, **wherein the 25-hydroxyvitamin D is administered in dosage amounts of from 1 to 100 µg per day, and wherein the intravenous administration is of 25-hydroxyvitamin D_2, 25-hydroxyvitamin D_3 or combinations thereof with other therapeutic agents.**"

Auxiliary request 3

1. **25-hydroxyvitamin D_3** for use in the treatment of hyperparathyroidism, wherein the **25-hydroxyvitamin D_3** is administered by intravenous delivery via controlled release, **and wherein the 25-hydroxyvitamin D_3 is administered in dosage amounts of from 1 to 100 µg per day to provide an average rise in serum 25-hydroxyvitamin D_3 of about 1 to 3 ng/mL.**"

III. According to the decision under appeal, claim 1 of the main request violated Articles 76(1) and 83 EPC, since there was no basis or disclosure for a controlled release intravenous composition of 25-hydroxyvitamin D.

In particular, the examining division observed that the application as originally filed did not disclose any controlled release composition of 25-hydroxyvitamin D suitable for intravenous injection.
Furthermore, the original application did not disclose any controlled release of 25-hydroxyvitamin D by intravenous delivery which was carried out by controlling the rate of intravenous feed into the body, as argued by the applicants.

The same conclusions applied to auxiliary requests 1-3.

IV. The applicants, (hereinafter the appellants) filed an appeal against said decision. They requested that the decision under appeal be set aside and the case be remitted to the examining division for further prosecution on the basis of the main request or one of auxiliary requests 1-3 filed with the statement setting out the grounds of appeal dated 5 October 2018. These requests correspond to those on which the decision of the examining division is based.

V. With the communication sent in preparation for oral proceedings, the Board expressed its preliminary opinion that the application did not fulfil the requirements of Article 83 EPC.

VI. With a letter dated 27 September 2020, the appellant filed auxiliary requests 4-7.

The subject-matter of claim 1 of auxiliary requests 4-7 was identical respectively to claim 1 of the main request and auxiliary requests 1-3. These requests differed from the main request and the auxiliary requests in the deletion of respectively dependent claims 10 and 11 for auxiliary request 4, dependent claims 9 and 10 for auxiliary request 5-6, and dependent claims 7 and 8 for auxiliary request 7.

VII. The appellant's arguments can be summarised as follows:

Article 83 EPC

Intravenous (IV) administration was known. Once the skilled person was told that he should treat hyperparathyroidism by IV administration of 25-hydroxyvitamin D as was disclosed in the application in

paragraph [0091], then he could have achieved this. The controlled release might be via an IV infusion to provide the active into the vein in a controlled manner over an extended period of time, in contrast to a bolus "push" of the active. The skilled person would be able to set up a controlled IV infusion feed or to use a IV syringe pump.

In addition, IV options were also available based on what was known in the art. For example, parenteral long-acting formulations had been in clinical use in the field of hormone replacement therapy for decades. Intravenous therapy was furthermore also known from textbooks.

Therefore the skilled person would be aware from his common general knowledge of details for potential IV administration systems. The claimed subject-matter was disclosed to the skilled person in a sufficient manner from reading the application as filed in light of his common general knowledge.

The requirement for sufficiency under the EPC did not necessitate that there was any type of specific information explicitly set out.

VIII. Requests

The appellants request that the decision under appeal be set aside and that the case be remitted to the examining division for further prosecution on the basis of the main request or one of auxiliary requests 1-3, all filed 5 October 2018 or one of auxiliary requests 4-7 filed with letter dated 27 September 2020.

Reasons for the Decision

1. Main request – Sufficiency of disclosure

1.1 The claimed invention relates to 25-hydroxyvitamin D for use in the treatment of hyperparathyroidism, wherein the 25-hydroxyvitamin D is administered by intravenous delivery via controlled release.

1.2 In order to fulfil the requirement of Art. 83 EPC, the application as filed must contain sufficient information to allow a person skilled in the art, using his common general knowledge, to carry out the invention within the whole area that is claimed.

1.3 The disclosure of the patent application relates to controlled release formulations, in particular to a solid or semi-solid waxy pharmaceutical formulation for controlled release of a vitamin for oral delivery (see par. [0002] or [0031]). Another disclosed aspect of the invention is a controlled release dosage that contains a phamacologically active amount of vitamin D compound and a release-modifying agent (see par. [0032]).

The application as filed makes constant reference to the delivery of the disclosed controlled release form in the gastrointestinal tract, or via oral administration and all concrete examples disclose oral capsules comprising a modified release formulation of said vitamin D compound (see also par. [0031], [0064], [0067], [0088]).

1.4 The description comprises two unique references as regards intravenous delivery of 25-hydroxyvitamin D, namely in paragraphs [0091] and [0111] of the original

application (paragraphs [0083] and [0103] of the published application EP 2 762 132 A1).

1.4.1 Paragraph [0091] discloses the following: "Advantageously, 25-hydroxyvitamin D2, 25-hydroxyvitamin D3 or combinations thereof together with other therapeutic agents can be orally or intravenously administered in accordance with the above described embodiments in dosage amounts of from 1 to 100 µg per day,…".

1.4.2 Paragraph [0111] discloses that "in addition, one may choose to intravenously administer 25-hydroxyvitamin D2 and/or 25-hydroxyvitamin D3 with cholecalciferol, ergocalciferol, active Vitamin D sterols,…".

1.4.3 Hence, these paragraphs do not disclose any specific formulation which could be used for controlled release via intravenous administration. Nor do these paragraphs provide any technical guidance on how a controlled release delivery of 25-hydroxyvitamin D could be achieved by intravenous administration. Accordingly, the description does not provide any information on how to perform the invention defined in claim 1.

1.5 In its submissions dated 27 September 2020, the appellant accepts that the application as filed does not provide a detailed set of instructions regarding the claimed subject-matter.

However, in its view, the general knowledge would compensate for the absence of a teaching of the description with regard to the preparation of intravenous controlled compositions of 25-hydroxyvitamin D. In this regard, in its statement setting out the grounds of appeal, the appellant

mentioned that parenteral long-acting formulations have been in clinical use in the field of hormone replacement therapy for decades, such as Delatestryl® (sesame oil-based injection containing testosterone enanthate), Delestrogen® (castor oil-based injection containing estradiol valerate), DepoProvera® (drug suspension for injection containing medroxyprogesterone acetate), Nutropin Depot® (long-acting injectable microspheres of recombinant growth hormone), as well as parenteral formulations of antipsychotic drugs in oil-based depot formulations and injectable PLGA microspheres for treating hormone-dependent cancers.

1.6 In this respect the Board observes that "parenteral" is not a synonym for "intravenous". It is a broad term used to define a route of administration that is not enteral. It includes for instance the intramuscular and subcutaneous administrations. The appellant has not provided any evidence that any of the formulations mentioned in its statement of grounds of appeal is a controlled release formulation for intravenous administration.

Moreover, these formulations represent very different and varied solutions for parenteral controlled release of drugs and are all very specific for a particular drug, and there are no elements which could suggest that these specific formulations may be suitable or adaptable for any other drug in general. In the present case, the appellants did not provide any evidence or credible argument that 25-hydroxyvitamin D could be incorporated in any type of the cited formulation and also be injected intravenously for providing a controlled release of 25-hydroxyvitamin D.

Thus, the fact that some parenteral long-acting formulations are known in the art does not help the skilled person seeking to carry out the invention defined in claim 1.

1.7 Following a different line of reasoning, the appellant argued that the skilled person is well aware that intravenous administration can be achieved via a controlled intravenous infusion feed over time, such as through a syringe pump, achieving thus a controlled release over an extended period of time.

However, any information or teaching as to a controlled infusion feed is not only entirely absent from the application as filed but is also not relevant. The present application refers indeed explicitly and consistently to controlled release compositions, i.e. to the controlled release or delivery of hydroxyvitamin D from a dosage form. On the other hand, the controlled intravenous infusion feed relates to the controlled administration of the drug and is unrelated to the aim and purpose of the present application.

Against this background, the citation of a textbook covering intravenous infusion therapy is also not relevant.

In any case, claim 1 covers the situation in which the controlled release effect is achieved by the use of a controlled release dosage form. Thus, arguing that the controlled release effect could be achieved also by a controlled administration cannot remedy the insufficiency of disclosure concerning the controlled release intravenous dosage form.

1.8 The main request does therefore not meet the requirements of Article 83 EPC.

2. Auxiliary requests 1-3

Claim 1 of these requests has been amended respectively by the features "wherein the 25-hydroxyvitamin D is administered in dosage amounts of from 1 to 100 µg per day", "wherein the 25-hydroxyvitamin D is administered in dosage amounts of from 1 to 100 µg per day, and wherein the intravenous administration is of 25-hydroxyvitamin D_2, 25hydroxyvitamin D_3 or combinations thereof with other therapeutic agents", and "wherein the 25-hydroxyvitamin D_3 is administered in dosage amounts of from 1 to 100 µg per day to provide an average rise in serum 25-hydroxyvitamin D3 of about 1 to 3 ng/mL".

These amendments have no impact on the conclusions reached above for the main request. Consequently, auxiliary requests 1-3 do not meet the requirements of Article 83 EPC.

3. Auxiliary requests 4-7

These requests correspond respectively to the the main request and auxiliary requests 1-3 with the deletion of dependent claims 10 and 11 for auxiliary request 4, dependent claims 9 and 10 for auxiliary request 5-6 and dependent claims 7 and 8 for auxiliary request 7.

Consequently, the conclusions reached above for the main request and auxiliary requests 1-3 apply mutatis mutandis and auxiliary requests 4-7 do not meet the requirements of Article 83 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated