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Datasheet for the decision of 28 October 2020

Case Number: T 1730/16 - 3.3.01

Application Number: 02795891.7

Publication Number: 1455796

IPC: A61K31/663, A61P19/10

Language of the proceedings: EN

Title of invention:
METHOD FOR THE TREATMENT OF BONE DISORDERS

Applicant:
Allergan Pharmaceuticals International Limited

Headword:
Risedronate dosage regime/ALLERGAN

Relevant legal provisions:
EPC Art. 56
EPC R. 103

Keyword:
Inventive step - (no)
Reimbursement of appeal fee at 25% - withdrawal of the request for oral proceedings

Decisions cited:
T 2044/16, T 0110/18

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Case Number: T 1730/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 28 October 2020

Appellant: (Applicant)	Allergan Pharmaceuticals International Limited Clonshaugh Industrial Estate Coolock Dublin 17 (IE)
Representative:	FRKelly 27 Clyde Road Dublin D04 F838 (IE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 30 November 2015 refusing European patent application No. 02795891.7 pursuant to Article 97(2) EPC**

Composition of the Board:

Chairwoman	G. Seufert
Members:	J. Molina de Alba
	M. Blasi

Summary of Facts and Submissions

I. By its decision posted on 30 November 2015, the examining division refused European patent application No. 02 795 891.7. The decision was based on the claims of a main request and three auxiliary requests.

II. The evidence cited during the examination and appeal proceedings includes the following documents.

D1 WO 01/15703
D5* E.S. Siris et al., Journal of Bone and Mineral Research, 13(6), 1998, 1032-1038
D6* B. Zegels et al., Bone, 28(1), 2001, 108-112
D11 A.J. Racewicz et al., Current Medical Research and Opinion, 23(12), 2007, 3079-3089
D12 Declaration of Ms T.M. de Vries dated 1 October 2015

III. In the decision, the examining division considered that the subject-matter of the requests on file lacked an inventive step over a combination of the teachings of documents D1 and D6*. In its reasoning, the examining division held, *inter alia*, that documents D11 and D12 did not show that the claimed dosage regime was advantageous over the one disclosed in D1.

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

With the statement of grounds of appeal, the appellant filed the claims of a main request and an auxiliary request identical to those of the main request and

auxiliary request 2 on which the appealed decision was based, respectively.

V. In line with the appellant's request, the board scheduled oral proceedings to be held on 28 May 2020.

In a communication pursuant to Article 15(1) RPBA 2007 annexed to the summons to oral proceedings, the board gave its preliminary opinion that the claimed subject-matter lacked an inventive step starting from document D1 or D5*.

VI. In response to the board's preliminary opinion, the appellant filed the claims of a new main request and auxiliary request to replace those previously on file.

Claims 1 and 4 of the main request read as follows.

"*1. A kit for use in treating high bone turnover comprising unit doses of bisphosphonate according to a regimen comprising a loading period and a maintenance period which follows the loading period, wherein the loading period unit doses are from 2 to 20 times per diem greater than the maintenance period unit doses and wherein the loading dose period is from 7 to 180 days, wherein the bisphosphonate is risedronate formulated for oral delivery, the loading period unit doses are from 15 mg to 50 mg per day and the maintenance period unit doses are from 2.5 mg to 15 mg per day.*"

"*4. A bisphosphonate for use in treating high bone turnover according to the steps of;*

a) administering a loading dose for 7 days to 180 days of a bisphosphonate; and

b) administering after step (a) a maintenance dose of a bisphosphonate wherein the loading dose is

from 2 to 20 times per diem greater than the maintenance dose,

wherein the bisphosphonate is risedronate formulated for oral delivery, the loading period unit doses are from 15 mg to 50 mg per day and the maintenance period unit doses are from 2.5 mg to 15 mg per day."

Claims 1 and 6 of the auxiliary request result from the addition of the sentence "*wherein equivalent doses can be given every other day, twice a week, weekly, bi-weekly or monthly*" at the end of claims 1 and 4 of the main request, respectively.

VII. In accordance with the restrictions imposed owing to the spread of coronavirus (COVID-19), the board postponed the date of the oral proceedings to 20 August 2020.

In preparation for the oral proceedings, the board sent a communication dated 9 July 2020 drawing attention to the COVID-19 constraints for oral proceedings held in person and the possibility of holding them via videoconference.

VIII. By a letter received on 5 August 2020, the appellant informed the board that it would not attend the oral proceedings and withdrew its request for oral proceedings.

IX. The oral proceedings were cancelled.

X. The appellant's arguments, where relevant to the present decision, may be summarised as follows.

The closest prior art is the treatment disclosed in document D1 rather than document D5*.

Should the treatment of document D5* nevertheless be taken as the starting point for the assessment of inventive step, the subject-matter of claim 1 of the main request differs from it in the dosage regime. The oral administration of risedronate at 30 mg/day for 84 days in D5* may be considered equivalent to the loading period of claim 1. However, the treatment of D5* does not contain a maintenance period following that loading period.

The technical effect produced by this difference is a faster decrease of bone turnover, which results in a faster increase of bone mass and a faster fracture reduction. This is proven by the data in document D11, as explained in declaration D12.

The objective technical problem is the provision of an improved treatment of high bone turnover using risedronate.

D5* neither discloses nor suggests a maintenance period following the loading period, let alone the benefits of it. Therefore, the subject-matter of the main request is inventive.

For the same reasons, the subject-matter of the auxiliary request is also inventive.

XI. The appellant requested that the decision under appeal be set aside and that a patent be granted based on the claims of the main request filed with the letter dated 28 April 2020 or, in the alternative, the claims of the auxiliary request filed on the same date.

Reasons for the Decision

1. The appeal is admissible. It complies with the requirements pursuant to Articles 106 to 108 and Rule 99(2) EPC.

2. In view of the appellant's withdrawal of the request for oral proceedings, and taking into consideration the appellant's written submissions and the board's preliminary opinion annexed to the summons to oral proceedings, the board was in a position to take a final decision without holding oral proceedings (Articles 113(1) and 116(1) EPC).

3. Main request - inventive step (Article 56 EPC)

3.1 The claims of the main request are directed to the treatment of high bone turnover by the oral administration of risedronate. This treatment is characterised by a dosage regime which comprises a loading period followed by a maintenance period, where the dose of risedronate during the loading period is 2 to 20 times greater than that of the maintenance period. In the loading period, risedronate is administered at 15-50 mg/day for 7-180 days while the dose during the maintenance period is 2.5-15 mg/day.

According to the application (page 2, paragraph 3), the administration of risedronate at a high dose followed by a lower maintenance dose decreases bone turnover and increases bone mass at a faster rate, leading to a faster fracture reduction.

3.2 The appellant regarded document D1 as the closest prior art and rejected the board's opinion that D5* was also a suitable starting point for the assessment of inventive step (see letter of 28 April 2020, page 13, paragraphs 4-5 from the bottom). It gave no reasons in this respect.

Whether or not document D5* is indeed the "closest" prior art in the sense that there is no other prior art closer than D5* is not relevant. For an inventive step to be acknowledged, the claimed subject-matter must be not obvious starting from anything forming part of the state of the art. Pursuant to Article 56 EPC, an invention is considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art. Excluded from the assessment are documents within the meaning of Article 54(3) EPC. D5* is not such a document.

3.3 D5* discloses (abstract) the treatment of Paget's disease of bone with oral risedronate. This disease is characterised by the occurrence of a high bone turnover, identified by particularly high serum levels of the marker alkaline phosphatase (ALP). In particular, the patients of D5* had initial mean serum ALP levels seven times the upper limit of normal.

In the treatment of D5*, risedronate was administered orally at 30 mg/day for 84 days, followed by a resting period of 112 days during which no risedronate was given. The administration of risedronate achieved a normalisation of serum ALP levels (i.e. a normalisation of bone turnover) that was maintained in the majority of patients for the whole resting period (see Figure 1), i.e. up to 196 days (84+112) from the start of the treatment. In the minority of patients whose serum ALP

was not normal or who had experienced a relapse by the end of the 196-day cycle, the treatment was repeated (D5*, abstract; page 1033, right-hand column, lines 7-9; and the "*Bone turnover*" section on pages 1034-1035). Moreover, the treatment was shown to be safe (D5, abstract and page 1036, "*Safety and tolerability*" section).

The dosage of 30 mg/day for 84 days in D5* falls within the definition of the loading period of claims 1 and 4, where the dose is 15-50 mg/day for 7-180 days.

The treatment of D5* is therefore a suitable starting point and has to be taken into consideration for assessing inventive step.

3.4 The appellant submitted that the difference between the treatment of claims 1 and 4 and that of D5* was that D5* does not disclose a maintenance period following the loading period (letter of 28 April 2020, page 13, last paragraph). The board agrees.

3.5 There is, however, no evidence on file showing the effect that this difference brings about.

According to the appellant, the difference provides an increase in bone mass at a faster rate (letter of 28 April 2020, page 14, paragraph 3). This view was based on the comparative examples in document D11, which were extensively discussed in the appellant's written submissions and declaration D12. However, these examples do not show any comparison between two dosage regimes comprising a loading period followed by either a maintenance period or a resting period.

The board concurs with the appellant that the loading period provides a fast reduction of bone turnover from the outset of the treatment. This is apparent from Figure 2 of D11, where the curve corresponding to the dosing of claims 1 and 4 shows an abrupt reduction of bone turnover to about 50% during the first month (loading period). After this loading period, during the following five months (maintenance period), bone turnover gradually recovers and stabilises at reduction levels of above 30%. This test, however, does not help to ascertain what would happen during the months following the loading period if a maintenance dose were not administered. Any conclusion on this would be purely speculative.

Moreover, although the experimental conditions of the treatments in D11 and D5* are not comparable, the result of the treatment of D5* was also a stabilisation of bone turnover at levels above 30% reduction during the months following risedronate administration (D5, page 1033, right-hand column, last paragraph, and page 1035, Figure 1).

Hence, the evidence on file does not let the board conclude that the administration of a maintenance dose following the loading period indeed results in an advantageous technical effect.

3.6 Therefore, the objective technical problem solved by the subject-matter of claims 1 and 4 is the provision of an alternative treatment of high bone turnover.

3.7 Knowing from D5* that the administration of risedronate at 30 mg/day for 84 days achieves the desired reduction of bone turnover and that this effect is maintained up to at least 6 months from the start of the treatment

(196 days are 6.5 months), the administration of a risedronate maintenance dose after day 84 would have been an obvious, if not superfluous, modification for the skilled person to provide an alternative treatment.

3.8 Hence, the subject-matter of claims 1 and 4 lacks an inventive step over the content of document D5*.

4. Auxiliary request - inventive step (Article 56 EPC)

Claims 1 and 6 of the auxiliary request derive from claims 1 and 4 of the main request, respectively, by the addition of the expression "*wherein equivalent doses can be given every other day, twice a week, weekly, bi-weekly or monthly*".

This additional expression merely recites an option (note the use of the verb "can") and is therefore not limiting. In consequence, the subject-matter of claims 1 and 6 of the auxiliary request is identical to that of claims 1 and 4 of the main request, respectively.

Thus, for the reasons put forward in relation to the main request, the subject-matter of claims 1 and 6 of the auxiliary request also lacks an inventive step.

5. Reimbursement of the appeal fee (Rule 103(4)(c) EPC)

The appellant had initially requested oral proceedings. The request was subsequently withdrawn, enabling the board to decide on the case without holding oral proceedings.

Pursuant to Rule 103(4)(c) EPC, in force since 1 April 2020, the appeal fee is to be reimbursed at 25% if any request for oral proceedings is withdrawn within

one month of notification of the communication issued by the board in preparation for the oral proceedings and no oral proceedings take place. The amended provision applies to any pending appeal pursuant to Article 2(2) of the Decision of the Administrative Council of 12 December 2019 amending Rule 103 EPC (CA/D 14/19, see OJ EPO 2020, A5), thus also to the present appeal case.

In the present case, the requirements for a reimbursement at 25% are met.

The appellant's withdrawal of its request for oral proceedings was received on 5 August 2020, i.e. within one month of notification of the board's communication dated 9 July 2020 (Rule 126(2), Rule 131(2) and (4) EPC).

Rule 103(4)(c) EPC does not specify particular criteria that a communication has to comply with for it to qualify for a possible reimbursement other than it must have been issued by the board "in preparation for the oral proceedings". The board's communication dated 9 July 2020 concerned technical and organisational aspects of the scheduled oral proceedings and is thus a communication issued in preparation for the oral proceedings (see also decision T 2044/16, point 5.3 of the Reasons).

A first communication pursuant to Article 15(1) RPBA having been issued by the board at a previous stage of the appeal proceedings is not prejudicial to a reimbursement of the appeal fee under Rule 103(4)(c) EPC.

Rule 103 EPC provides the legal basis for a reimbursement in full or part and is not concerned with setting a minimum or maximum number of communications which can or should be issued by the board. Thus, the board interprets the definite article in Rule 103(4)(c) EPC ("notification of the communication") as not being associated with a limitation as to board's number of communications but - seen in the context of the provision as a whole - merely as referring to the previous mentions of "a communication" in Rule 103(3)(a) and (b) EPC.

In addition, the board agrees with the findings in decisions T 2044/16 and T 110/18 that allowing a reimbursement in circumstances such as the present ones, i.e. where the withdrawal of the request for oral proceedings occurred after a second (or further) communication was issued, is in line with the purpose for which the provision of Rule 103(4)(c) EPC was created (see T 2044/16, point 5.5 of the Reasons; T 110/18, point 7 of the Reasons with reference to CA/80/19, point 82).

Accordingly, the appellant is entitled to a reimbursement of the appeal fee at 25%.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

2. The appeal fee is reimbursed at 25%.

The Registrar: The Chairwoman:

M. Schalow G. Seufert

Decision electronically authenticated