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Datasheet for the decision of 22 September 2020

Case Number: T 1712/17 - 3.3.07

Application Number: 04759349.6

Publication Number: 1615646

IPC: A61K9/08, A61K45/06, A61K47/12, A61K47/18, A61K9/19, A61K31/047, A61K31/195, A61K31/485

Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL FORMULATIONS CONTAINING METHYLNALTREXONE

Patent Proprietor:
PROGENICS PHARMACEUTICALS, INC.

Opponents:
Actavis Group PTC ehf
Fresenius Kabi Deutschland GmbH

Headword:
Pharmaceutical Formulations Containing Methylnaltrexone / PROGENICS

Relevant legal provisions:
RPBA Art. 12(4)
EPC Art. 123(2), 84
RPBA 2020 Art. 11

Keyword:
Late-filed request - request identical to request not admitted in first instance proceedings - admitted (yes)
Amendments - extension beyond the content of the application as filed (no)
Remittal to the department of first instance - special reasons for remitting the case

Decisions cited:
T 1966/16

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Case Number: T 1712/17 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 22 September 2020

Appellant: (Patent Proprietor)	PROGENICS PHARMACEUTICALS, INC. 777 Old Saw Mill River Road Tarrytown, NY 10591 (US)
Representative:	Maiwald Patent- und Rechtsanwaltsgesellschaft mbH Elisenhof Elisenstraße 3 80335 München (DE)
Respondent: (Opponent 1)	Actavis Group PTC ehf Reykjavikurvegi 76-78 220 Hafnarfjördur (IS)
Representative:	Ter Meer Steinmeister & Partner Patentanwälte mbB Nymphenburger Straße 4 80335 München (DE)
Respondent: (Opponent 2)	Fresenius Kabi Deutschland GmbH Else-Kröner-Str. 1 61352 Bad Homburg (DE)
Representative:	Fresenius Kabi Deutschland GmbH Patent Department Borkenberg 14 61440 Oberursel (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 28 June 2017 revoking European patent No. 1615646 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	E. Duval
	Y. Podbielski

Summary of Facts and Submissions

I. European Patent 1615646 (hereinafter "the patent") was granted on the basis of 13 claims.

Claim 1 of the patent as granted read as follows:

"*A pharmaceutical preparation comprising a solution of methylnaltrexone or a salt thereof and a chelating agent, wherein the chelating agent is ethylenediaminetetraacetic acid (EDTA) or a derivative thereof, niacinamide or a derivative thereof, or sodium desoxycholate or a derivative thereof.*"

II. Two oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step and it extended beyond the content of the application as filed.

III. The opposition division took the decision to revoke the patent.

The decision was based on the patent as granted as main request, on auxiliary requests I and II filed by letter dated 7 July 2016, on auxiliary requests III and IV filed by letter dated 29 March 2017, and on auxiliary requests V and VI filed by letter dated 24 May 2017. The opposition division did not admit into the proceedings auxiliary request VII filed during the oral proceedings.

IV. The opposition division decided in particular as follows:

(a) The main request did not meet the requirements of Article 123(2) EPC, because claim 1 did not contain the feature that the concentration of methylnaltrexone degradation products did not exceed 2% of the methylnaltrexone or salt thereof in the preparation. Auxiliary requests I and II infringed Article 123(2) EPC for the same reason.

(b) Auxiliary request III met the requirements of Articles 123(2) and (3) EPC. However, claim 1 was found unclear for lack of information as to what the percentage of methylnaltrexone degradation products referred to. Auxiliary requests IV-VI failed to meet the requirements of clarity of Article 84 EPC for the same reason.

(c) Auxiliary request VII was filed late and did not *prima facie* meet the requirements of Article 123(2) EPC. Accordingly, the opposition division did not admit auxiliary request VII into the proceedings.

V. The patent proprietor (appellant) lodged an appeal against the decision of the opposition division.

With its statement setting out the grounds of appeal, the appellant defended its case on the basis of the patent as granted as main request, and on the basis of auxiliary requests I, II, III, IV, V, Va, VI, VIa, VII, VIII and IX filed therewith.

Auxiliary request VII was identical to the auxiliary request VII filed during the oral proceedings before the opposition division. It comprised a sole claim 1 reading as follows:

"*A pharmaceutical preparation comprising a solution of methylnaltrexone or a salt thereof and a chelating agent, wherein the chelating agent is ethylenediaminetetraacetic acid (EDTA) or a derivative thereof, wherein the EDTA or derivative thereof is present in a concentration from 0.1 to 25.0 mg/ml, and wherein the pH is from 2.0 to 4.0.*"

VI. Both respondents 1 (opponent 1) and 2 (opponent 2) replied to the appeal.

VII. In a communication under Article 15(1) RPBA, the Board expressed its preliminary opinion.

VIII. Oral proceedings were held before the Board in the presence of the appellant only. Neither respondent 1 nor respondent 2 attended the oral proceedings, as announced respectively in their letters dated 18 September 2019 and 4 May 2020.

In the course of the oral proceedings, the appellant made auxiliary request VII its main request.

IX. The appellant's arguments as regards auxiliary request VII (now pursued as the main request) can be summarised as follows:

(a) The conclusion of the opposition division according to which auxiliary request VII did not *prima facie* overcome the objections under Article 123(2) EPC was not correct (see (b) below). Hence auxiliary request VII should be admitted into the proceedings.

(b) Auxiliary request VII found basis, for the purposes of Article 123(2) EPC, in claims 1, 11, 12 and 23

of the application as filed, as well as page 2, lines 16-18. Claim 1 of the main request did not contain the feature that the concentration of methylnaltrexone degradation products did not exceed 2% of the methylnaltrexone or salt thereof in the preparation. However this feature was made redundant by the limitation to a pH of 2.0 to 4.0 and to an amount of EDTA or derivative thereof of 0.1 to 25.0 mg/ml, as taught in the description of the application as filed, page 12 lines 14-15 and 30-32, and page 13, line 28 to page 14, line 15. Hence the feature regarding a concentration of methylnaltrexone degradation products of at most 2% could be dispensed with.

Alternatively, auxiliary request VII found basis in the last paragraph on page 3 of the application as filed, in combination with page 6, lines 4-6, page 14, lines 11-15, and page 2, lines 9-12 for the chelating agent; page 2 and claims 11-12 for the EDTA concentration; page 3, lines 30-31 and claim 23 for the pH range.

X. The respondents' arguments as regards auxiliary request VII can be summarised as follows:

(a) Auxiliary request VII should not be admitted into the proceedings. The opposition division had exercised its discretion in an appropriate way, by finding that auxiliary request VII did not meet the requirements of Article 123(2) EPC (see (b) below). The Board should therefore not overrule the way in which the opposition division had exercised its discretion.

(b) The subject-matter of auxiliary request VII was not disclosed on page 3 of the application as filed. Said passage on page 3, lines 18-26 defined a solution of methylnaltrexone in a degradation inhibiting agent, and not a preparation comprising a solution of methylnaltrexone or salt thereof and a chelating agent as in auxiliary request VII.

Furthermore, said passage of the application as originally filed contained further features such as the amount of degradation inhibiting agent, the stability of the composition or its processing under at least one sterilisation technique, which were missing from auxiliary request VII.

Lastly, the preparation of auxiliary request VII covered embodiments in which the pH and/or the EDTA concentration were not sufficient to provide a low amount of methylnaltrexone degradation products after autoclaving.

Claims 11 and 12 could not function as pointers for the claimed EDTA concentration, as they were dependent on claim 1 which also contained the stability criteria regarding the amount of methylnaltrexone degradation products, in accordance with the aspect described on page 2. Similarly, claim 23 of the application as originally filed was not a pointer for the claimed pH range, as it was also dependent on claim 1. The stability criteria of claim 1 could not be omitted without infringing Article 123(2) EPC.

Accordingly, auxiliary request VII did not meet the requirements of Art 123(2) EPC.

XI. The following requests are relevant to this decision:

The appellant requests that the decision under appeal be set aside and that the case be remitted to the opposition division for further prosecution on the basis of auxiliary request VII filed with the statement setting out the grounds of appeal.

Respondents 1 and 2 request that the appeal be dismissed. Respondent 1 further requests that auxiliary request VII not be admitted into the proceedings.

Reasons for the Decision

Auxiliary request VII (pursued as the main request)

1. Admittance into the proceedings

The appellant submitted auxiliary request VII together with its statement setting out the grounds of appeal, which was filed before 1 January 2020. Following the transitional provisions set out in Article 25(2) RPBA 2020, the admittance of auxiliary request VII must be decided on the basis of Article 12(4) RPBA 2007. Article 12(4) RPBA 2007 gives the Board discretion not to admit, on appeal, requests which could have been presented or were not admitted in the first instance proceedings.

1.1 Auxiliary request VII was filed during the oral proceedings in opposition. The opposition division did not admit auxiliary request VII into the proceedings. Nonetheless, the Board retains its own margin of discretion to admit auxiliary request VII upon appeal, pursuant to Article 12(4) RPBA 2007.

1.2 Auxiliary request VII is aimed at overcoming the opposition division's finding that auxiliary requests III-VI did not comply with the requirements of Article 84 EPC. As noted by the appellant, in the course of the proceedings before the opposition division, the clarity objection was raised for the first time during the oral proceedings. In these circumstances, the Board sees the filing of auxiliary request VII as justified by the developments in the first-instance proceedings.

Accordingly, auxiliary request VII is admitted into the proceedings.

2. Article 123(2) EPC

2.1 As basis for claim 1 of auxiliary request VII, the appellant cites among others claims 1, 11, 12 and 23 of the application as filed.

The Board notes that claim 1 of auxiliary request VII differs from claim 1 of the application as filed by the addition of the features pertaining to
- the presence of a chelating agent being EDTA or a derivative thereof,
- the concentration range of from 0.1 to 25.0 mg/ml for said EDTA or derivative thereof, and
- the pH range of from 2.0 to 4.0,
and by the deletion of the feature "wherein the preparation after autoclaving has a concentration of methylnaltrexone degradation products that does not exceed 2% of the methylnaltrexone or salt thereof in the preparation".

2.2 The Board considers that both the presence of EDTA or derivative thereof as chelating agent and its

concentration range of from 0.1 to 25.0 mg/ml find basis in claims 11 and 12 of the application as filed. The presence of EDTA or derivative thereof as chelating agent is required by claims 11-12, and by claims 7 and 8 on which they depend. In addition, claim 11 discloses a broad concentration range of 0.05 to 25.0 mg/ml for EDTA or its derivative, whereas claim 12 discloses a more preferred range of 0.1 to 2.5 mg/ml. According to established case law, in the case of such a disclosure of both a general and a preferred range, a combination of the preferred disclosed narrower range and one of the part-ranges lying within the disclosed overall range on either side of the narrower range is unequivocally derivable from the original disclosure of the patent in suit and thus supported by it (see Case Law of the Boards of Appeal, 9th edition, July 2019, II.E.1.5.1). The concentration range of 0.1 to 25.0 mg/ml of auxiliary request VII is thus derived directly and unambiguously from claims 11 and 12.

Furthermore, the pH range of 2.0 to 4.0 is disclosed in dependent claim 23, or, alternatively, on page 2, lines 16-18.

2.3 Claim 1 of auxiliary request VII omits the feature of claim 1 of the application as filed according to which "the preparation after autoclaving has a concentration of methylnaltrexone degradation products that does not exceed 2% of the methylnaltrexone or salt thereof in the preparation". The Board however agrees with the appellant that, in view of the teaching of the application as filed, this feature is made redundant by the limitations pertaining to the pH of 2.0 to 4.0 and the concentration range of from 0.1 to 25.0 mg/ml for the EDTA or derivative thereof, for the following reasons.

2.3.1 Regarding the pH, the application as filed on page 12, lines 14-15 and 30-32 indicates that "pH alone can solve the problem of excessive methylnaltrexone degradation products" and teaches the effect of a pH below 4.25 (thus encompassing the claimed range of 2.0-4.0) on the amount of methylnaltrexone degradation products following autoclaving.

2.3.2 As to the choice and amount of EDTA or derivatives thereof as chelating agent, page 13, lines 28-29, indicates that "a chelating agent alone was capable of reducing the amount of degradation product to acceptable levels". In the same paragraph, disodium edetate is said to stabilize methylnaltrexone against heat degradation in a concentration-dependent manner, and a concentration of 0.1 mg/ml already results in under 1.5% (hence less than 2%) total degradants (page 14, line 2). This result is generalised to EDTA and derivatives in the following paragraph (page 14, line 13).

2.3.3 Consequently, it is directly and unambiguously derivable from the application as filed as a whole that the selection of the claimed pH range and concentration range for EDTA or derivatives leads to a concentration of methylnaltrexone degradation products that does not exceed 2%. This teaching is not contradicted by any passage of the application as filed. In particular, the conditions under which more than 2% degradants were observed (i.e. a pH between 6.0 and 7.0, cf. page 14 lines 25-28; or a concentration of 0.01 mg/ml of sodium edetate, cf. page 14, line 1) are not covered by claim 1 of auxiliary request VII.

Respondent 1 expressed the view that the preparation claimed in auxiliary request VII covered embodiments in which the pH and/or the EDTA concentration were not sufficient to provide a low amount of methylnaltrexone degradation products after autoclaving. However, the application as filed does not disclose such embodiments. The Board stresses that, for the purposes of Article 123(2) EPC, the relevant question is whether the application as filed teaches that the features of the amended claim lead to the fulfillment of the omitted feature (that is the feature pertaining to the concentration of methylnaltrexone degradation products that does not exceed 2% after autoclaving). The question is not whether this teaching is verified by facts.

Therefore, the omission of the feature relating to the methylnaltrexone degradation products that does not exceed 2% satisfies the "gold standard", and remains within the limits of what the skilled person would regard as directly and unambiguously derivable from the application as filed.

2.4 The appealed decision found the subject-matter of auxiliary request VII to result from multiple selections. Although this reasoning was based on different passages of the application as filed (namely page 3), the Board emphasizes that the application as filed provides support for the combination of the above features.

Thus, the opposition division considered that the presence of EDTA or derivative thereof as chelating agent resulted from several selections, namely the selection of a chelating agent out of the possible methylnaltrexone degradation inhibiting agents, and the

selection of EDTA or derivative thereof from the list of chelating agents. The Board does not agree. The choice of EDTA or derivative thereof necessarily entails the presence of this chelating agent in the preparation. Hence this feature does not involve multiple selections within two *independent* lists of alternative features.

Furthermore, the passages of the application as filed discussed above (see 2.3.1 and 2.3.2), which emphasize the effect of the selected pH range, chelating agent and amount thereof on the extent of degradation of methylnaltrexone, can be seen as pointers to the combination of these features.

2.5 In conclusion, auxiliary request VII meets the requirements of Article 123(2) EPC.

3. Clarity

The respondents did not raise any objection regarding the clarity of auxiliary request VII. The Board considers that the amendments do not introduce any non-compliance with Article 84 EPC.

4. Remittal to the opposition division

Under Article 11 RPBA 2020 the board may remit the case to the department whose decision was appealed if there are special reasons for doing so. In the present case, the opposition division decided only on the question of added subject-matter and clarity. There is no appealable decision regarding the further grounds for opposition under Article 100(a) EPC. In these circumstances, the Board considers that special reasons for remitting the case to the opposition division exist

(see T 1966/16, point 2). Therefore, the Board considers it appropriate to accede to the appellant's request for a remittal.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the opposition division for further prosecution.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated