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Datasheet for the decision of 24 February 2021

Case Number: T 2232/17 - 3.3.04

Application Number: 05768245.2

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Language of the proceedings: EN

Title of invention:
Natalizumab for use in treating diseases needing steroid treatment

Patent Proprietor:
Biogen MA Inc.

Opponent:
Pharmaceutical Works Polpharma SA

Headword:
Natalizumab for diseases treatable with steroids/BIOGEN

Relevant legal provisions:
EPC Art. 100(a), 54
EPC R. 103(1)(a), 111(1)
RPBA Art. 12(4)
RPBA 2020 Art. 11

Keyword:

Decisions cited:
T 0388/09, J 0009/10, T 1101/92, T 1198/97, T 2373/11, G 0007/93, T 0231/85, T 1642/06, T 2251/14, T 0836/01, T 0019/86, T 0893/90, T 1399/04, T 0734/12, G 0002/88, T 1127/02

Catchword:

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Case Number: T 2232/17 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 24 February 2021

Appellant: (Patent Proprietor)	Biogen MA Inc. 225 Binney Street Cambridge, MA 02142 (US)
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Representative:	Wichmann, Hendrik Wuesthoff & Wuesthoff Patentanwälte PartG mbB Schweigerstraße 2 81541 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 26 July 2017 revoking European patent No. 1734997 pursuant to Article 101(3)(b) EPC**

Composition of the Board:

Chairman	A. Chakravarty
Members:	B. Rutz
	M. Blasi

Summary of Facts and Submissions

I. An appeal was lodged by the patent proprietor (appellant) against the decision of the opposition division to revoke European patent No. 1 734 997. The patent is entitled "*Natalizumab for use in treating diseases needing steroid treatment*". The opponent is respondent to this appeal.

II. The patent was opposed on the grounds set out in Article 100(a) EPC, in relation to novelty (Article 54 EPC) and inventive step (Article 56 EPC), and also those set out in Article 100(b) and (c) EPC.

III. In the decision under appeal, the opposition division held that claims 1 to 17 of the main request complied with the requirements of Article 123(2) EPC, but that the invention to which claim 1 related was not sufficiently disclosed (Article 83 EPC) with regard to any diseases other than Crohn's disease and multiple sclerosis (MS).

IV. With regard to auxiliary request 1, the opposition division held that the claims complied with the requirements of Article 123(2), (3) and Articles 84 and 83 and Rule 80 EPC. The subject-matter of claim 1 was found to be novel over the disclosure in document D3, but lacked novelty over the disclosure in document D4 (Article 54 EPC).

V. With regard to auxiliary request 2, the opposition division held that the claims as amended complied with Article 84 EPC and the invention to which the claims related was sufficiently disclosed (Article 83 EPC).

The subject-matter of claim 1 was held to lack novelty over the disclosure in document D4 (Article 54 EPC).

VI. With regard to auxiliary requests 3 to 5, the opposition division held that claim 7 of these claim requests did not meet the requirements of Article 123(2) EPC.

VII. During oral proceedings, the opposition division decided not to give the appellant the opportunity to submit sets of claims of alternative auxiliary requests 3 to 5 because they would have been filed late, holding that their subject-matter was "*likely to have an impact on the consideration of sufficiency of disclosure*" and that "*there was no reason to expect that this ground of opposition* [inventive step] *was going to be solved in favour of the Patentee*" (see decision under appeal, point 29).

VIII. The events preceding the non-admittance of alternative auxiliary requests 3 to 5 can be summarised as follows.

An objection to added subject-matter in dependent claim 10 of the main request was raised by the respondent one week before oral proceedings before the opposition division. This objection was considered by the respondent also to apply to claim 8 of auxiliary request 1 and to claim 7 of each of auxiliary requests 2 to 5 (see letter dated 27 June 2017, point II). The set of claims of the main request had initially been filed as auxiliary request 1 with the reply to the notice of opposition, the other auxiliary requests were filed on 3 May and 2 June 2017.

During said oral proceedings, the opposition division agreed with this objection and held claim 10 of the

then main request to contain added subject-matter (see minutes, point 3.5).

The appellant reacted to this by requesting to file sets of claims of a new main and auxiliary requests 1 to 5, addressing the issue of added subject-matter by deletion of the relevant dependent claims. Only the new main request, replacing the then main request, was admitted by the opposition division and "[t]*he chairman indicated that the P would subsequently be given the opportunity to react during the course of the proceedings by filing further requests as and when appropriate*" (see minutes, point 4.).

Later during the oral proceedings, before auxiliary requests 1 and 2 were dealt with, the appellant filed new auxiliary requests 1 and 2, as replacements for the then auxiliary requests 1 and 2. These auxiliary requests contained the same deletion of the dependent claim as the main request and were admitted into the proceedings by the opposition division.

After the opposition division held new auxiliary requests 1 and 2 to be not allowable for lack of novelty, they announced that the claims of each of auxiliary requests 3 to 5 did not comply with Article 123(2) EPC for the same reasons as the original main request. Subsequently, the appellant requested to file replacement requests in which the added subject-matter issue had been corrected (see minutes, point 7.4.2).

The opposition division then informed the appellant that it refused to admit the further claim requests (see minutes, point 7.4.3).

IX. With the statement of grounds of appeal, the appellant filed sets of claims of a main request and 17 auxiliary requests.

X. The respondent replied to the appeal.

XI. The board appointed oral proceedings as requested by the parties and in a communication pursuant to Article 15(1) RPBA 2020, informed the parties of its preliminary opinion on the appeal.

XII. With their reply to the board's communication, the appellant filed sets of claims of auxiliary requests 18 to 26 and document D35.

XIII. Oral proceedings before the board took place on 24 February 2021. The hearing was held as a mixed-mode videoconference with the consent of the parties. The appellant was present in person while the respondent attended remotely. During the oral proceedings and in view of the board's decision not to admit the main and auxiliary requests 1 and 2 as filed with the statement of grounds of appeal into the proceedings under Article 12(4) RPBA 2007, the appellant renumbered the claim requests by promoting former auxiliary requests 9 to 13 to main request and auxiliary requests 1 to 4, respectively, and demoting former auxiliary requests 3 to 8 to auxiliary requests 5 to 10, respectively, and demoting former auxiliary requests 14 to 26 to auxiliary requests 11 to 23, respectively. At the end of the oral proceedings, the chair announced the board's decision.

XIV. Independent claim 1 of the main request reads:

"1. Use of natalizumab or an immunologically active fragment thereof for the preparation of a medicament to be administered to a human subject in a steroid sparing effective amount to reduce and/or eliminate a need for steroid treatment in the human subject with a disease selected from the group consisting of inflammatory bowel disease, asthma, multiple sclerosis, graft versus host disease, host versus graft disease, spondyloarthropathies, and combinations thereof, wherein the human subject is under treatment with steroids."

Independent claim 1 of auxiliary request 1 reads:

"1. Use of natalizumab or an immunologically active fragment thereof for the preparation of a medicament to be administered to a human subject in a steroid sparing effective amount to reduce and/or eliminate a need for steroid treatment in the human subject with a disease selected from the group consisting of Crohn's disease and multiple sclerosis, wherein the human subject is under treatment with steroids."

Independent claim 1 of auxiliary request 2 reads:

"1. Use of natalizumab or an immunologically active fragment thereof for the preparation of a medicament to be administered to a human subject in a steroid sparing effective amount to reduce and/or eliminate a need for steroid treatment in the human subject with a disease selected from the group consisting of Crohn's disease and multiple sclerosis, wherein the human subject is under treatment with steroids, wherein the human subject is refractory, intolerant or dependent on

steroids and wherein natalizumab is administered in an amount effective to permit the human subject to be tapered from steroid therapy."

XV. The following documents are cited in this decision:

D4 WO 03/072040

D21 Way Back Machine capture of http://partnersmscenter.org:80/treatment.html (from the Multiple Sclerosis Center Brookline, MA), from February 16, 2006

D22 R. Sadovsky, "Tips from other journals: Managing Steroid-Dependent Crohn's Disease", American Family Physician, 2004, 69(4):971-972

D33 Multiple Sclerosis, National clinical guideline for diagnosis and management in primary and secondary care; Royal College of Physicians of London; ISBN 1 86016 182 0; Section 4: Disease diagnosis and specific treatment, Glossary and List of References, 2004

D34 R. Zivadinov et al., "Effects of IV methylprednisolone on brain atrophy in relapsing-remitting MS", Neurology, 2001, 57:1239-1247

D35 J. E. Joy and R. B. Johnston, Jr. (eds.), "Multiple Sclerosis: Current Status and Strategies for the Future", Institute of Medicine, The National Academy Press, 2001, pages 390-399

XVI. Appellant's arguments as far as relevant to the present decision are summarised as follows.

Main request and auxiliary requests 1 and 2, all submitted with the statement of grounds of appeal

Admission in the appeal proceedings (Article 12(4) RPBA 2007)

The main request and auxiliary requests 1 and 2 had not been explicitly and unconditionally withdrawn during oral proceedings before the opposition division. Instead, it was attempted to have them replaced with auxiliary requests 9 to 11 in which the objected dependency or claim was deleted. Under the present circumstances, the appellant was entitled to pursue these claims on appeal (see Case Law Book, 8th edition, 2016, IV.E.4.3.2(d)) and decisions T 937/11 and T 883/12).

Main request and auxiliary request 1 (submitted with the statement of grounds of appeal as auxiliary requests 9 and 10, respectively)

Claim construction - claim 1

Claim 1 contained the following features:

(A) Use of natalizumab or an immunologically active fragment thereof for the preparation of a medicament
(B) to be administered to a human subject in a steroid sparing effective amount to reduce and/or eliminate a need for steroid treatment
(C) in the human subject with a disease selected from the group consisting of inflammatory bowel disease, asthma, multiple sclerosis, graft versus host disease,

host versus graft disease, spondyloarthropathies, and combinations thereof,
(D) wherein the human subject is under treatment with steroids.

Features (B) and (D) were of particular importance to distinguish the subject-matter from the prior art.

"*to reduce and/or eliminate a need for steroid treatment in the human subject*"

The reasoning in decision G 2/88 (supplemented by T 231/85 and T 1642/06) should be applied to the previously unknown effect of steroid reduction for natalizumab in the inflammatory conditions mentioned in claim 1 (feature (B), above). The steroid sparing effect of natalizumab was a functional feature and was clearly not derivable from the prior art. Moreover, it represented a significant and improved treatment regimen elucidated and enabled for the first time by the present invention. The medical use was the administration of natalizumab (in a steroid sparing effective amount) to patients having one of the diseases mentioned in the claim with the purpose to reduce and/or eliminate the need for steroid treatment.

"*under treatment with steroids*"

From a number of passages in the patent (see paragraphs [0016], [0019-0020], [0043], [0054], [0154], [0375], [0389], [0394-0395]), it was clear that the human subject was already undergoing steroid treatment when natalizumab was administered. The expression also included the situation where therapy with natalizumab had completely eliminated the need for steroids because the subject was "under treatment with steroids" when

the natalizumab treatment was started. Claim 1 did not necessarily require that the steroids are administered "on the same day" as the treatment with natalizumab, but it could not include patients who had not received any corticosteroid treatment within 30 days, as for example disclosed in document D4. On the other hand, a dosage regimen such as the one disclosed in document D34 in which patients are given intravenous methylprednisolone pulses every 4 months, did fall under the term "under treatment with steroids".

Novelty (Article 54 EPC) - claim 1

In the decision under appeal the opposition division held that the subject-matter of claim 1 was not novel with respect to MS over document D4. However, document D4 did not disclose the treatment as claimed of patients suffering from MS. In particular, it did not disclose reducing or eliminating steroids by using natalizumab. Moreover, the study described in Example 1 of document D4 excluded MS patients who had taken steroids within 30 days of natalizumab administration. Thus, no treatment of patients "under treatment with steroids" was disclosed.

Auxiliary request 2 (submitted with the statement of grounds of appeal as auxiliary request 11)

Novelty (Article 54 EPC) - claim 1

Document D4 did not anticipate the subject-matter of claim 1 because it did not disclose the group of patients specifically identified in the claim, i.e. a "human subject [which] is refractory, intolerant or dependent on steroids". With regard to the interpretation of the term "dependent on steroids"

paragraph [0008] of the patent ("*Patients taking steroids may be come* [sic] *dependent, intolerant or refractory to steroids*") should be taken into account. The word "become" made it clear that a specific development was meant which occurred only in some patients. Document D22 which was published before the priority date (February 2004) indicated that "patients with steroid-dependent Crohn's disease are those who respond to steroid therapy but cannot taper the treatment". The fact that the patients in the study in Example 1 of document D4 had not received systemic corticosteroids within the past 30 days clearly indicated that these MS patients were not dependent upon steroid treatment.

Auxiliary requests 3 and 4 (submitted with the statement of grounds of appeal as auxiliary requests 12 and 13)

Admission in the appeal proceedings (Article 12(4) RPBA 2007) and reimbursement of the appeal fee (Rule 103(1)(a) EPC)

The appellant was prevented from presenting claim requests to overcome the opposition division's decision on the patentability of the considered claim requests. Amended auxiliary requests 3 to 5 filed in the proceedings before the opposition division were in direct response to a late added subject-matter objection and should have been considered. In light of the opposition division's decision on added subject-matter of claim 10 of the main request of 3 May 2017 at oral proceedings, these claim requests were also filed in time. The non-admittance of these claim requests by the opposition division contravened Article 113(1) EPC and constituted a substantial procedural violation

which warranted reimbursement of the appeal fee (Rule 103 EPC).

XVII. Respondent's arguments as far as relevant to the decision may be summarised as follows.

Main request and auxiliary requests 1 and 2, all submitted with the statement of grounds of appeal

Admission in the appeal proceedings (Article 12(4) RPBA 2007)

The main request and auxiliary requests 1 and 2 were replaced during the oral proceedings before the opposition division by an amended main request and amended auxiliary requests 1 and 2. This could only be interpreted as a withdrawal of the former requests. The original claim requests should therefore not be admitted into the appeal proceedings.

Main request and auxiliary request 1 (submitted with the statement of grounds of appeal as auxiliary requests 9 and 10, respectively)

Claim construction - claim 1

"*to reduce and/or eliminate a need for steroid treatment in the human subject*"

This expression in claim 1 belonged to the definition of the effective amount of natalizumab and not to the definition of the medical indication. It constituted an (inherent) feature of the amount of natalizumab administered which simply expressed the possibility that less steroid could be administered to the subject. However, it was not to be understood as limiting the

claimed subject-matter to a dosage regimen including a step of reducing the amount of steroid administered. The feature in the claim related to the mere possibility of reducing the amount of steroids administered which represented a purely mental act. Thus, the "*therapeutically effective amount*" defined in paragraph [0053] was identical to the "*steroid sparing effective amount*" defined in paragraph [0054] of the patent.

Claim 1 also did not require a multi-step dosage regimen in which steroids were replaced by natalizumab. Rather, it reflected a single point in time in the treatment of a human subject with both natalizumab and steroids when the "need" for steroids was actually reduced or eliminated.

It followed from this that the subject-matter of claim 1 was the same as the prior art merely expressed in different words.

Finally, the claimed medical use related only to the administration of natalizumab (in a steroid sparing effective amount) to patients having one of the diseases mentioned in the claim.

"*under treatment with steroids*"

The patent was silent about the initiation or start of the treatment with natalizumab. It also did not require the subject to be "treatment naive". Therefore a subject "under treatment with steroids" in the sense of the claim was one who received steroids at any time before or during the administration of natalizumab. An MS patient who relapsed while being treated with natalizumab and was consequently given a short-term

treatment with steroids had to be considered as "under treatment with steroids".

Novelty (Article 54 EPC) - claim 1

Example 1 on page 37 of document D4 described a controlled trial of natalizumab in relapsing MS. According to lines 20 to 25 on page 37, the patients received six infusions of 6 mg/kg or 3 mg/kg natalizumab at 28 day intervals, which was a steroid sparing effective amount to reduce and/or eliminate the need for steroid treatment in the sense of the patent. The statement "*more relapses ... than in the treated arms*" on page 42, lines 1 to 4, implied that at least some of the patients treated with natalizumab must have received short-term treatment with steroids. This was in accordance with page 29, lines 25 to 27 of document D4, which stated that "[s]*hort-term use of either adrenocorticotropic hormone (ACTH) or oral corticosteroids (e.g., oral prednisone or intravenous methylprednisolone) is the only specific therapeutic measure for treating patients with acute exacerbation of MS.*" These patients were thus concomitantly treated with both natalizumab and steroids. Once the symptoms of the acute relapse diminished, it was inherently disclosed that natalizumab was administered in an amount effective to further reduce or even eliminate the need for steroid treatment.

Auxiliary request 2 (submitted with the statement of grounds of appeal as auxiliary request 11)

Novelty (Article 54 EPC)

There was, in the context of treating MS, no generally recognised definition in the art of a subject

refractory, intolerant or dependent on steroids. Neither document D21 or D22 provided such a definition either. Document D21 could not provide evidence for common general knowledge at the time of the priority date because it was published later, and anyway did not provide a definition of steroid dependent MS patients. Document D22 was not concerned with MS. Hence, these terms must be given the broadest possible interpretation (see e.g. T 1127/02, point 7 of the Reasons). Moreover, document D33, the UK national clinical guideline for MS did not mention "dependent" in its glossary.

Any subject being treated with steroids during an acute relapse in MS was "dependent on steroids" in that moment. Even if this group of steroid dependent MS patients could be distinguished from the group of MS patients in general, an MS patient dependent on steroids was already disclosed in Example 1 of document D4.

Auxiliary requests 3 and 4 (submitted with the statement of grounds of appeal as auxiliary requests 12 and 13)

Admission in the appeal proceedings
(Article 12(4) RPBA 2007)

Auxiliary requests 3 and 4 in which dependent claim 7 (corresponding to claim 10 as granted) had been deleted were intended to be filed by the appellant during the oral proceedings before the opposition division, but had not been admitted into the proceedings. In accordance with established case law of the boards of appeal, the board was limited to review the opposition division's exercise of its discretion under

Rule 116(2) EPC. The opposition division had not exceeded the proper limits of its discretion such that a further detailed discussion of auxiliary requests 3 and 4 was not necessary.

XVIII. The appellant requested that the decision under appeal be set aside and the patent be maintained in amended form based on the claims of the main request, filed as auxiliary request 9 with the statement of grounds of appeal or alternatively, on the basis of one of the sets of claims of auxiliary requests 1 to 14 filed as auxiliary requests 10 to 13, 3 to 8 and 14 to 17 with the statement of grounds of appeal, respectively or further alternatively, on the basis of auxiliary requests 15 to 23, filed as auxiliary requests 18 to 26 with the letter dated 23 December 2020. The appellant further requested that the board remit the case to the opposition division for further prosecution and that the appeal fee be reimbursed pursuant to Rule 103(1)(a) EPC in view of a substantial procedural violation committed by the opposition division.

XIX. The respondent requested that the appeal be dismissed or alternatively, that the case be remitted to the opposition division for further prosecution. The respondent further requested that all requests other than the main request and auxiliary requests 1 and 2 (former auxiliary requests 9 to 11) be excluded from the proceedings under Article 12(4) RPBA 2007 or not be admitted into the proceedings, respectively.

Reasons for the Decision

Main request and auxiliary requests 1 and 2, all submitted with the statement of grounds of appeal

Admission in the appeal proceedings (Article 12(4) RPBA 2007)

1. Pursuant to Article 12(4) RPBA 2007, the board has the power to hold inadmissible requests which could have been presented in the proceedings before the opposition division even though they have been submitted with the statement of grounds of appeal. In the board's opinion, the provision applies *a fortiori* to requests which were presented in opposition but subsequently withdrawn because, as in the cases explicitly addressed in the provision, the opposition division was likewise prevented from taking a decision on these requests.

2. The sets of claims of the main and auxiliary requests 1 and 2 as submitted with the statement of grounds of appeal are identical to the sets of claims of the main request and auxiliary requests 1 and 2 as filed with the appellant's letter dated 3 May 2017. According to the minutes of the oral proceedings before the opposition division, these claim requests were replaced at the oral proceedings by a new main request and auxiliary requests 1 and 2, respectively (see minutes, top of pages 4 and 9, points 5.1.4 and 7.4.2). Thus, the main request and auxiliary requests 1 and 2 as filed on 3 May 2017 were effectively withdrawn. This is confirmed by the fact that the appellant designated the claim requests submitted at the oral proceedings (see minutes, Annexes I, IV and V) with the same designations as the replaced ones and that a clarification of the hierarchy of requests, which would have been necessary if there had been colliding

designations, was not minuted. Nor was a correction of the minutes requested by the appellant. In view of these circumstances, the board concludes that the main and auxiliary requests 1 and 2 as filed with the statement of grounds of appeal were withdrawn at the oral proceedings before the opposition division.

3. In view of the above and taking into account that the primary object of the appeal proceedings is to review the decision under appeal in a judicial manner (see Article 12(2) RPBA 2020), the board decided to hold the main and auxiliary requests 1 and 2, as filed with the statement of grounds of appeal, inadmissible pursuant to Article 12(4) RPBA 2007.

Main request (submitted as auxiliary request 9 with the statement of grounds of appeal)

Claim construction - claim 1

4. Claim 1 is directed to a second or further medical use and drafted in the Swiss-type format.

5. The claim was interpreted differently by the parties with regard to the meaning of (i) "to be administered to a human subject in a steroid sparing effective amount to reduce and/or eliminate a need for steroid treatment in the human subject with a disease selected from the group ..." (see sections XVI. and XVII. above) and (ii) the patient group to be treated ("the human subject is under treatment with steroids").

6. In respect of feature (i), the board considers that "to reduce and/or eliminate a need for steroid treatment", does not define a different clinical situation to that in which this feature would be absent. This is because

reducing the need for treatment only defines a situation which may or may not lead to a difference in treatment. The underlying medical use defined in claim 1 is therefore not different from the administration of natalizumab in the absence of any considerations about the need for steroid treatment. In other words, the feature "to reduce and/or eliminate the need for steroid treatment" does not limit the subject-matter of the claim.

7. The appellant argued that "*the technical effect of steroid reduction remained hidden* [in the prior art] *and can form the basis of a novel medical use*" and that "[t]*he functional feature of the steroid sparing effect of natalizumab is clearly not derivable from the prior art and represents a significant and improved treatment regimen elucidated and enabled for the first time by the present invention*" (letter of 23 December 2020, points 37 and 41, respectively).

8. However, the board's claim construction is in line with the established case law, e.g. in decision T 836/01 the competent board held that a "*new technical effect would have to lead to a truly new industrial/commercial application (see e.g. decision G 5/83, point 16) arising from e.g. the opening a new field of application, the healing of a different pathology/ clinical situation, the creation of a distinct group or sub-group of subjects (either end-users or patients) or the new use must involve new physical means/measures for its practise*" (see point 8 of the Reasons, which was followed by, for example T 2251/14, and endorsed by the Enlarged Board of Appeal in G 2/08, see point 6.3 of the Reasons).

9. In relation to feature (ii) the board considers that, in the absence of a definition in the patent, the skilled person would give the expression "under treatment with steroids" its broadest technically sensible meaning, including the administration of natalizumab and steroids at separate time points. Administration of steroids to patients under treatment with natalizumab in reaction to acute events (e.g. relapses) is thus encompassed by the expression.

10. The appellant submitted that the wording of the claim made it "*clear that the human subject is under treatment with steroids when the natalizumab therapy is initiated*" (statement of grounds of appeal, point 97). The appellant, however, also agreed with the interpretation of the opposition division that "*there seems to be no reason to interpret the expression 'under treatment with steroids' in a restrictive manner which would require intake of the steroids the same day that the treatment with natalizumab starts*" (see point 12.2 of the decision under appeal and points 98 and 99 of the statement of grounds of appeal). During oral proceedings before the board, the appellant further stated that a treatment in which pulsed intravenous methylprednisolone was given to patients with MS "*every 4 months for 3 years and then every 6 months for the subsequent 2 years*" (see document D34, Abstract) fell under the definition of "under treatment with steroids" referred to in claim 1.

11. Therefore, the board concludes that the medical use to which claim 1 relates is the administration of natalizumab or an immunologically active fragment thereof to a human subject with a disease selected from the group of specified diseases, wherein the human subject is under treatment with steroids (including the

administration of natalizumab and steroids at separate time points) and wherein the amount of natalizumab used is such that it is therapeutically effective and hence allows (but does not require) a reduction or elimination of steroids.

Novelty (Article 54 EPC)

12. In the decision under appeal, the subject-matter of claim 1 of auxiliary request 1, filed as auxiliary request 10 with the statement of grounds of appeal, was held to lack novelty over the disclosure of document D4 (points 12.1 and 12.2 of the decision) with respect to treatment of MS. This subject-matter is also an embodiment of claim 1 of the main request.

13. Example 1 on page 37 of document D4 discloses the treatment of patients suffering from relapsing MS with natalizumab. The patients received six infusions of 6 mg/kg or 3 mg/kg natalizumab at 28 day intervals. In the paragraph "*Clinical efficacy outcome*" it is stated that "[*m*]*ore relapses in the placebo group required steroid treatment than in the treated arms (22 in placebo, 5 in the 3 mg/kg natalizumab, and 7 in the 6 mg*/kg natalizumab groups" (page 42, lines 1 to 4). From this it can be taken that at least some patients treated with natalizumab received short-term treatment with steroids, namely at the time when relapses occurred. Document D4 therefore discloses a human subject under treatment with steroids at a time when natalizumab was administered.

14. The board further considers that the amount of natalizumab administered to patients in document D4 was "steroid sparing" as construed in point 6. above. The amount of 3 mg/kg or 6 mg/kg of natalizumab in

Example 1 of document D4 lies within the dose range defined in the patent as "steroid sparing amount" for inflammatory bowel diseases ("2mg/kg to 8mg/kg", see claim 10 as granted). It also corresponds to the fixed dosage of 300 mg used in the clinical trials disclosed in the patent for Crohn's disease (see paragraph [0372]). The appellant in the context of sufficiency of disclosure referred to paragraph [0349] in the patent which reads: "*Thus, since the 3 mg/kg dose was efficacious in both CD and MS indications, the 6 mg/kg dose resulted in no evidence of dose-limiting toxicities and there was no added benefit of the 6 mg/kg dose over the 3 mg/kg dose, a 300 mg fixed dose is an appropriate choice for Phase III studies.*" The appellant further stated that the skilled person would use the same fixed dose of 300 mg in both diseases, Crohn's and MS. The board thus concludes that the patent discloses that the "steroid sparing amount" for MS can be the same as for Crohn's disease, namely 3 mg/kg or 300 mg fixed dose. In any case, the amount of natalizumab administered in example 1 of document D4 (3mg/kg or 6mg/kg) led to a reduction in the number of relapses (see point 13. above), i.e. it showed a steroid sparing effect.

15. Document D4 thus discloses a human subject suffering from MS "under treatment with steroids" and being treated with natalizumab in a "steroid sparing amount".

16. The subject-matter of claim 1 lacks novelty over the disclosure of document D4. The requirements of Article 54 EPC are thus not met.

Auxiliary request 1 - claim 1

Novelty (Article 54 EPC)

17. The subject-matter of claim 1 differs from that of claim 1 of the main request in that the diseases are limited to Crohn's disease and MS. Since the above arguments with regard to novelty of claim 1 of the main request relate to MS as an embodiment of the claimed subject-matter, they apply equally. The claimed subject-matter lacks novelty. The requirements of Article 54 EPC are thus not met.

Auxiliary request 2 - claim 1

Novelty (Article 54 EPC)

18. The subject-matter of claim 1 differs from that of claim 1 of the main request and of auxiliary request 1 in that the human subject to be treated is further defined as "refractory, intolerant or dependent on steroids" and in that the administration of natalizumab is further specified to be "in an amount effective to permit the human subject to be tapered from steroid therapy".

19. The patent contains no definition of the expression "dependent on steroids". The appellant referred to paragraph [0008]: "*Patients taking steroids may be come* [sic] *dependent, intolerant or refractory to steroids.*" as evidence that a patient becomes "dependent on steroids" as a result of a process occurring during treatment with steroids and that the patient group defined in the claim does not include patients given steroids to treat a relapse. The board is however of the view that the skilled person, giving the words

their ordinary meaning, would consider the group of patients "dependent" on steroids to include those who depend on them in any way, including dependency because no alternative treatments are available, such as those being treated with natalizumab who suffer a relapse of the disease and are then treated with steroids. The board has seen no disclosure in the patent or forming part of the common general knowledge that would serve to support a narrower definition.

20. Documents D21 and D22 were cited by the appellant as evidence that the skilled person's common general knowledge led to a particular understanding of the expression "dependent on steroids". However, the appellant's arguments are not persuasive for two reasons: Firstly, Document D21 was published after the filing date of the patent and thus cannot serve as evidence of common general knowledge. Secondly, document D22 defines "[p]*atients with steroid-dependent Crohn's disease*" as those "*who respond to steroid therapy but cannot taper the treatment*". Notwithstanding the fact that document D22 relates to Crohn's disease and not to MS, the conclusion from this document is that patients "dependent on steroids" need and respond to steroids and thus cannot taper (i.e. reduce or eliminate) the treatment. Thus, document D22 does not support a different construction of the expression "dependent on steroids" than the one set out in point 19. above.

21. In view of the above claim construction, the patients disclosed in document D4 who received natalizumab and were treated with steroids for relapses are considered "dependent on steroids".

22. It is established case law of the boards of appeal that the use of the same compound in the treatment of the same disease for a particular group of subjects can represent a new therapeutic application, provided that it is carried out on a new group of subjects which is distinguished from the known group by its physiological or pathological status (see e.g. T 19/86, OJ EPO 1989, 24, point 8 of Reasons; T 893/90, point 4.2 of Reasons; T 1399/04, point 35 of Reasons and T 734/12, point 24 of Reasons). In the present case, the board has seen no evidence that patients suffering from MS and who are "dependent on steroids" differ in their physiological or pathological status from the general group of MS patients, in particular with respect to their suitability for being treated with natalizumab. The patent contains no data on the treatment of MS patients with steroids and/or natalizumab. Moreover, even if the patent was taken as disclosing a sub-group of "steroid dependent" patients, no special therapeutic or pharmacological effect of natalizumab in this sub-group is disclosed in the patent. Thus, even if the patients disclosed in document D4 were not considered to be dependent on steroids, this feature would not establish novelty.

23. The second difference between claim 1 of auxiliary request 2 and claim 1 of the main request is a further definition of the amount of natalizumab administered to the patient. However, the board cannot see a difference in substance between the "steroid sparing amount to reduce and/or eliminate a need for steroid treatment in the human subject" of claim 1 of the main request and "an amount effective to permit the human subject to be tapered from steroid therapy" of claim 1 of auxiliary request 2. Indeed, the appellant pointed out that "tapering[...] requires a reduction over time" (see

statement of grounds of appeal, point 134.). Both the term "permit" in the present claim and the phrase "reducing or eliminating a need" in claim 1 of the main request do not limit the claimed use to one in which reduction of steroids is actually required. Instead, both phrases only describe that the use makes a reduction of steroids possible. The above mentioned second difference therefore represents a functional feature, inherent in the dose of natalizumab disclosed in document D4 (3 mg/kg or 6 mg/kg).

24. The board therefore agrees with the finding of the opposition division that the subject-matter of claim 1 of auxiliary request 2 is not novel over the disclosure of document D4. The requirements of Article 54 EPC are thus not met.

Auxiliary requests 3 and 4

Admission in the appeal proceedings (Article 12(4) RPBA 2007)

25. The sets of claims of auxiliary requests 3 and 4, filed as auxiliary requests 12 and 13 together with the statement of grounds of appeal, are identical to the sets of claims of auxiliary requests 3 and 4 as filed in opposition with letter dated 2 June 2017, respectively, except that dependent claim 7 has been deleted in each claim set. It can be taken from the opposition division's explanations (see decision and minutes) and the parties' submissions, that they represent two of the three claim requests which the appellant attempted to submit at the oral proceedings before the opposition division, but the submission of which was not permitted by the division.

26. According to established case law, a board of appeal should only overrule the way in which a department of first instance exercised its discretion under Article 114(2) EPC, if the board concludes that it has done so according to the wrong principles, or without taking into account the right principles, or in an unreasonable way (see also G 7/93, OJ EPO 1994, 775, point 2.6 of the Reasons).

27. In the present case, the opposition division rejected auxiliary requests 3 to 5 as filed with letter dated 2 June 2017 by relying on an issue of added subject-matter in a dependent claim (see minutes, point 7.4.1 and decision, points 23 to 25). The contentious subject-matter was in fact already present in the claims as granted, as well as in all claim requests submitted throughout the opposition proceedings. However, a corresponding objection to the main and auxiliary requests 1 to 5 then on file was raised by the respondent only one week before the oral proceedings.

28. For the main and auxiliary requests 1 and 2, the opposition division allowed the appellant to react to this late objection by deletion of the relevant parts in the dependent claims. However, in relation to auxiliary requests 3 to 5 which had likewise already been on file before this added subject-matter objection was raised and which the opposition division considered as admitted into the proceedings (see decision under appeal, point 27.2), it did not allow the deletion of the dependent claim but considered them as not allowable for the sole reason of added subject-matter in a dependent claim (see decision, points 23 to 25).

29. A first reason provided by the opposition division as to why it admitted some claim requests in which the objection under Article 123(2) EPC was addressed but not others, was that "*the discussion of three claim requests submitted during the oral proceedings represent a fair opportunity for the Proprietor to defend its case effectively*" and that "[a] *Patentee's right to be heard does not include a guarantee that all the requests prepared will be considered, regardless of their number*" (see point 27 of the decision).

30. Apart from the deleted dependent claim, the sets of claims of the auxiliary requests 3 to 5 intended to be filed by the appellant were identical to those of auxiliary requests 3 to 5 which had been admitted into the opposition proceedings. The opposition division's consideration that the appellant had already been given several opportunities during the oral proceedings to submit auxiliary requests does not appropriately take into account that the auxiliary requests 3 to 5 as filed with letter dated 2 June 2017 had been submitted to address other objections raised at earlier stages of the opposition proceedings, in the absence of the knowledge of the objection under Article 123(2) EPC relating to the respective dependent claim. The board therefore does not find this reason convincing.

31. As a further reason, the opposition division referred to the long duration of the oral proceedings and the late point in time (21:35 hours) when the appellant attempted to file the sets of claims of alternative auxiliary requests 3 to 5 (see point 27.1 of the decision). The board however notes that the appellant had attempted to replace all auxiliary request at an early stage of the oral proceedings (see minutes, point 4., "New Main Request") which was not permitted

by the opposition division. Also this reason is therefore not considered pertinent.

32. Finally, the opposition division reasoned that "*the individualisation of the patient sub-groups was likely to have an impact in the consideration of sufficiency of disclosure, as the data in the patent was limited to the three sub-groups identified initially mixed together. Moreover, inventive step had not been discussed at all, and there was no reason to expect that this ground of opposition was going to be solved in favour of the Patentee.*" (see point 29 of the decision). However, the amendment by way of deletion of the dependent claim was the same in all of the claim requests which the appellant attempted to file at the oral proceedings and cannot be seen to have led to new issues or increase the complexity of the case. Potential issues under sufficiency of disclosure and inventive step were identical between the admitted auxiliary requests 3 to 5 and the non-admitted requests and can therefore not justify the non-admittance.

33. In view of the above, the board considers that the opposition division exercised their discretion in an unreasonable way, preventing the appellant from pursuing alternative auxiliary claim requests 3 to 5 which were intended to address issues with regard to sufficiency of disclosure, novelty and inventive step.

34. This course of action amounts to a substantial procedural violation since the reason for rejecting auxiliary requests 3 to 5 then on file was one which the appellant had not been given an opportunity to address and since this rejection had an immediate impact on the outcome of the opposition.

35. The board therefore decided to set aside the opposition division's decision not to admit auxiliary requests 3 and 4 into the proceedings and to take them into account in these appeal proceedings in accordance with Article 12(4) RPBA 2007.

Remittal to the opposition division (Article 111(1) EPC)

36. Pursuant to Article 111(1) EPC, following the examination as to the allowability of the appeal the board may either exercise any power within the competence of the department which was responsible for the decision appealed or remit the case to that department for further prosecution. Under Article 11 RPBA 2020 the case is not remitted for further prosecution unless special reasons present themselves for doing so.

37. The opposition division has not decided on the substantive issues with regard to auxiliary request 3 and lower ranking auxiliary requests. The board would next have to consider at least the requirements of Articles 83 and 56 EPC which may be considered as being interrelated. However, neither inventive step nor a number of the documents cited by the respondent as closest prior art (e.g. documents D5, D7, D10 and D34) were dealt with in the decision under appeal. Moreover, both parties requested the remittal of the case to the opposition division for further prosecution. Thus, the board considers that special reasons within the meaning of Article 11 RPBA 2020 present themselves and it therefore decides to remit the case to the opposition division for further prosecution.

Reimbursement of appeal fee (Rule 103 EPC)

38. According to Rule 103(1)(a) EPC the appeal fee is to be reimbursed in full where the board of appeal deems an appeal to be allowable, if such reimbursement is equitable by reason of a substantial procedural violation. In order to render the reimbursement of the appeal fee equitable, a causal link must exist between the alleged procedural violation and the decision of the opposition division that necessitated the filing of an appeal (see also J 9/10, point 3.1 of Reasons).

39. In the present case, the opposition division rejected the main request for lack of sufficiency of disclosure and the auxiliary requests 1 and 2 for lack of novelty. When dealing with these requests, no substantial procedural violation had occurred and indeed the appellant did not argue this. These requests were maintained in appeal. The appellant would therefore have had to file an appeal in relation to these claim requests and the board, having regard to these circumstances, cannot establish any causal link between the need to file an appeal and the substantial procedural violation such that the reimbursement could be regarded as equitable.

40. The request for reimbursement of the appeal fee is therefore rejected.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

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

The Registrar: The Chairman:

I. Aperribay A. Chakravarty

Decision electronically authenticated