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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

YEDA RESEARCH & DEVELOPMENT CO. LTD.,
Patent Owner.

Case IPR2015-00644
Patent 8,399,413 B2

Before SHERIDAN K. SNEDDEN, ZHENYU YANG, and TINA E. HULSE, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Mylan Pharmaceuticals Inc. ("Petitioner") filed a corrected Petition requesting an *inter partes* review of claims 1–20 of U.S. Patent No. 8,399,413 B2 (Ex. 1001, "the '413 patent"). Paper 8 ("Pet."). Yeda Research & Development Co. Ltd. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 12 ("Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon considering the Petition and Preliminary Response, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–20. Accordingly, we institute an *inter partes* review of those claims.

A. Related Proceedings

Petitioner states that it is a defendant in several litigations involving the '413 patent. Pet. 2. Petitioner also identifies numerous other cases against other defendants involving the '413 patent. *Id.*

Petitioner has also filed petitions for *inter partes* review of related patents in IPR2015-00643 (US 8,232,250 B2) and IPR2015-00830 (US 8,969,302 B2).

B. The '413 Patent

Multiple sclerosis ("MS") is a chronic, autoimmune disease of the central nervous system. Ex. 1001, 1:16–18. There are five main forms of MS, including Relapsing-Remitting Multiple Sclerosis ("RRMS"). *Id.*

at 1:29. Patients suffering from RRMS experience sporadic exacerbations or relapses, as well as periods of remission. *Id.* at 1:30–31.

Glatiramer acetate ("GA" or "copolymer-1") is a mixture of polypeptides that do not all have the same amino acid sequence, and is marketed as Copaxone ®. *Id.* at 1:53–54. Administering 20 mg per day of Copaxone is an FDA-approved therapy for patients with RRMS. *Id.* at 2:13–16. The '413 patent discloses "an effective low frequency dosage regimen of GA administration to patients suffering from a relapsing form of [MS], including patients who have experienced a first clinical episode and have MRI features consistent with [MS]." *Id.* at 2:43–47. The disclosed method comprises administering to a patient suffering from RRMS three subcutaneous injections of a therapeutically effective dose of GA over a period of seven days with at least one day between every subcutaneous injection so as to thereby alleviate a symptom of the patient. *Id.* at 2:51–60.

C. Illustrative Claim

Petitioner challenges claims 1–20 of the '413 patent. Claim 1 is illustrative and is reproduced below:

> 1. A method of reducing the frequency of relapses in a human patient suffering from relapsing-remitting multiple sclerosis or a patient who has experienced a first clinical episode and has MRI features consistent with multiple sclerosis comprising administering to the human patient a therapeutically effective dosage regimen of three subcutaneous injections of 1 ml of a pharmaceutical composition comprising 40 mg of glatiramer acetate over a period of seven days with at least one day between every subcutaneous injection, the regimen being sufficient to reduce the frequency of relapses in the patient.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–20 of the '413 patent on the following grounds:

References	**Basis**	**Claims challenged**
Pinchasi[1]	§ 102	1–6 and 8–20
Pinchasi	§ 103	1–20
Pinchasi and the 1996 SBOA[2]	§ 103	1–20
Pinchasi and Flechter[3]	§ 103	1–20

II. ANALYSIS

A. Person of Ordinary Skill in the Art

The parties dispute the proper definition of a person of ordinary skill in the art. Petitioner contends that a person of ordinary skill in the art would have had (1) several years of experience in the pharmaceutical industry or in practicing medicine; (2) experience with the administration or formulation of therapeutic agents, dosing schedules and frequencies, and drug developmental study and design; and (3) a Ph.D. in pharmacology or be a physician with experience in clinical pharmacology. Pet. 12. Patent Owner disagrees with Petitioner's definition because it does not include experience

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[1] Irit Pinchasi, WO 2007/081975 A2, published July 19, 2007 (Ex. 1005).

[2] Summary Basis of Approval ("SBOA") for the New Drug Application for 20 mg daily Copaxone ® (NDA #20-622) (Ex. 1007).

[3] S. Flechter et al., *Copolymer 1 (Glatiramer Acetate) in Relapsing Forms of Multiple Sclerosis: Open Multicenter Study of Alternate-Day Administration*, 25 CLINICAL NEUROPHARM. 11–15 (2002) (Ex. 1008).

with MS or GA, which, according to Patent Owner, are both requirements for a person of ordinary skill in the art. Prelim. Resp. 34–35.

We agree with Patent Owner that a person of ordinary skill in the art should have experience with MS and GA. We note that one of Petitioner's declarants, Dr. Ari Green, states that a person of ordinary skill in the art would have "direct experience administering therapeutic agents for the treatment of MS, as well as familiarity with the dosing schedules and frequencies of the different therapeutic agents available for MS treatment." Ex. 1004 ¶ 27. Patent Owner does not otherwise dispute Petitioner's definition. Prelim. Resp. 34–35.

Accordingly, we adopt Petitioner's definition of a person of ordinary skill in the art, with the addition that that person would also have experience with MS and GA.

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. *See In re Cuozzo Speed Techs., LLC*, No. 2014-1301, 2015 WL 4097949, at *5–*8 (Fed. Cir. July 8, 2015); 37 C.F.R. § 42.100(b). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Each of the claims of the '413 patent recites administering a "therapeutically effective dosage regimen of three subcutaneous injections

of 1 ml of a pharmaceutical composition comprising 40 mg of glatiramer acetate over a period of seven days with at least one day between every subcutaneous injection." The parties dispute whether the claims encompass a dosage regimen that can include more than three subcutaneous injections within seven days, or if they are limited to a dosage regimen with only three subcutaneous injections over seven days. Petitioner argues the former construction, whereas Patent Owner argues the latter.

More specifically, Petitioner argues that the use of the open-ended "comprising" transition supports its proposed construction. Pet. 14. Petitioner also argues that the term "a regimen," which is not defined by the Specification, does not limit the open-ended nature of "comprising." *Id.* at 14–15. Thus, Petitioner concludes that "the use of the open-ended transition 'comprising' coupled with the use of the indefinite article 'a' before 'regimen' reinforces that the independent claims are each open-ended and allow for additional, unrecited elements to fall within the scope of the claim." *Id.* at 15.

Patent Owner disagrees. Patent Owner argues that Petitioner improperly uses the "comprising" transition to "reach into subsequent individual method step limitations and render each of them open-ended." Prelim. Resp. 28–29 (citing *Dippin' Dots, Inc. v. Mosey*, 476 F.3d 1337, 1343 (Fed. Cir. 2007)). Patent Owner also argues that the applicant expressly disclaimed dosage regimens with alternate-day administration during prosecution. As noted by Patent Owner, the examiner rejected the claims as anticipated by Flechter, which discloses administration of copolymer-1 "in an alternate-day administration schedule for up to two years." *Id.* at 24–25 (quoting Ex. 1002, 92). In response, the applicant amended the claims to require a therapeutically effective "regimen," and

argued that Flechter did not disclose "a 'regimen' requiring administration 3 times during a seven day period because the treatment protocol of Flechter et al. results in four administrations every other successive seven day period." *Id.* (quoting Ex. 1002, 186) (emphasis omitted). In other words, the applicant expressly disclaimed Flechter's alternate-day administration of copolymer-1.

At this stage of the proceeding, we are persuaded that Patent Owner's construction constitutes the broadest reasonable interpretation of the claims. We agree with Patent Owner that, while the term "comprising" allows for additional steps in the claimed method, the term does not "reach into each [limitation] to render every word and phrase therein open-ended." *Dippin' Dots*, 476 F.3d at 1343. Thus, we do not find that the term "comprising" requires us to construe the claims to encompass more than three subcutaneous injections of 40 mg of GA over a period of seven days, as Petitioner contends.

Moreover, in determining the broadest reasonable interpretation of a claim, the Federal Circuit stated that we cannot construe claims "so broadly that [our] constructions are *unreasonable* under general claim construction principles." *See Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1298 (Fed. Cir. 2015). Thus, the court instructed that we should "also consult the patent's prosecution history in proceedings in which the patent has been brought back to the agency for a second review." *Id.*; *see also Tempo Lighting, Inc. v. Tivoli, LLC*, 742 F.3d 978 (Fed. Cir. 2014) (affirming the Board's application of prosecution history disclaimer). Here, we agree with Patent Owner that, during prosecution, the applicant clearly disavowed administering the drug on alternate days by amending and distinguishing its claims over the prior art.

Accordingly, we determine that the broadest reasonable interpretation of the claims does not encompass a dosage regimen that alternates days over a period of seven days (i.e., one that administers the drug three times in one week and four times the next).

C. Anticipation by Pinchasi

Petitioner asserts that claims 1–6 and 8–20 are anticipated by Pinchasi. Pet. 20–45. Petitioner relies on the testimony of two declarants, Dr. Stephen J. Peroutka (Ex. 1003) and Dr. Ari Green (Ex. 1004). Patent Owner opposes Petitioner's assertion. Prelim. Resp. 32–33. Based on the current record, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the claims are anticipated by Pinchasi.

1. Pinchasi (Ex. 1005)

Pinchasi is a published PCT application that relates to a method of alleviating a symptom of a patient suffering from a relapsing form of MS. Ex. 1005, 9.[4] The method comprises periodically administering by subcutaneous injection a 40 mg dose of GA. *Id.* Pinchasi discloses that the GA can be administered daily or every other day. *Id.* Pinchasi also discloses that the alleviated symptom can be the frequency of relapses. *Id.*

2. Analysis

Petitioner argues that Pinchasi discloses each limitation of claims 1–6 and 8–20. For example, for independent claims 1, 19, and 20, Petitioner argues that Pinchasi's disclosure of 40 mg injections of GA every other day

[4] Unless stated otherwise, we cite to the unique page numbers provided by the parties in the lower right hand corner of the exhibits, pursuant to 37 C.F.R. 42.63(d)(2). For purposes of clarity, we suggest the parties do the same in future filings.

discloses the limitation requiring three injections over seven days with at least one day in between every injection. Pet. 22–26. As explained above, however, we do not construe the claims so broadly. That is, at this stage of the proceeding, we determine that the broadest reasonable interpretation of each of the claims does not encompass Pinchasi's disclosure of GA injections every other day. Accordingly, we conclude that Petitioner has failed to establish a reasonable likelihood that it would prevail in showing that Pinchasi anticipates claims 1–6 and 8–20.

D. Obviousness over Pinchasi and the 1996 SBOA

Petitioner argues that claims 1–20 are unpatentable as obvious over Pinchasi and the 1996 SBOA. Pet. 51–55. Patent Owner opposes. Prelim. Resp. 34–53. Based on the current record, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing claims 1–20 are unpatentable over Pinchasi and the 1996 SBOA.

1. The 1996 SBOA (Ex. 1007)

The 1996 SBOA is a compilation of documents relating to the Summary Basis of Approval for the New Drug Application ("NDA") for 20 mg Copaxone®. The compilation includes a review and evaluation of clinical data submitted by the sponsor of the NDA, Teva Pharmaceuticals, USA ("Teva"). Ex. 1007, 24–124. It also includes a review of the pharmacology and toxicology studies submitted by Teva. *Id.* at 125–292. The NDA was approved on December 20, 1996. *Id.* at 4.

2. Analysis

a. Whether the 1996 SBOA Is Prior Art

As support for its contention that the 1996 SBOA is prior art, Petitioner included a declaration from Marlene S. Bobka, the president of FOI Services, Inc., which provided the 1996 SBOA to Petitioner.

Ex. 1007, 1. Ms. Bobka states that FOI Services specializes in U.S. Food & Drug Administration ("FDA") information and "maintains a private library of over 150,000 FDA documents obtained under the Freedom of Information Act." *Id.* Ms. Bobka further states that FOI Services sells the documents and provided the 1996 SBOA to Petitioner on July 17, 2007. *Id.*

Patent Owner argues that this evidence is not sufficient for Petitioner to establish that the 1996 SBOA is a "printed publication" under 35 U.S.C. § 102(b). Prelim. Resp. 48–49. Specifically, Patent Owner argues that the 1996 SBOA was not published by the FDA, and that Ms. Bobka's declaration is insufficient to show that the 1996 SBOA was publicly available before the earliest possible priority date of the '413 patent. Prelim. Resp. 49–50.

At this stage of the proceedings, we are persuaded that Petitioner has set forth sufficient evidence that the 1996 SBOA constitutes prior art to the '413 patent. That is, we are persuaded—for purposes of this Decision—that the 1996 SBOA was sufficiently accessible to the public at least by July 17, 2007, when Ms. Bobka states FOI Services provided the 1996 SBOA to Petitioner, and which is before the earliest possible critical date of the '413 patent (i.e., August 20, 2008). *See Voter Verified, Inc. v. Premier Election Solutions*, 698 F.3d 1374, 1380 (Fed. Cir. 2012) ("[T]he key inquiry is whether the reference was made 'sufficiently accessible to the public interested in the art' before the critical date.'") (quoting *In re Cronyn*, 890 F.2d 1158, 1160 (Fed. Cir. 1989)).

b. Obviousness Analysis

Petitioner asserts that claims 1–20 are unpatentable as obvious over Pinchasi and the 1996 SBOA. For example, regarding claim 1, Petitioner asserts that Pinchasi discloses each limitation of the claim, except for the

dosing regimen of three doses per seven day period. Specifically, Petitioner argues that Pinchasi teaches the preamble of claim 1 by disclosing that the invention provides a method of alleviating a symptom of a patient suffering from a relapsing form of MS, where the symptom is the "frequency of relapses." Pet. 21 (citing Ex. 1005, 8:2–4, 14–15). Regarding the dosage amount, Petitioner asserts that Pinchasi teaches administering a subcutaneous injection of a pharmaceutical composition comprising 40 mg of GA and 40 mg of Mannitol USP in 1 mL sterilized water. *Id.* at 22–23 (citing Ex. 1005, 5:2–8, 13:21–24, Example 1). Based on the current record, we are persuaded that Petitioner has shown sufficiently that Pinchasi teaches each limitation of claim 1, except the dosing frequency.

Petitioner argues that the dosing frequency would have been obvious over Pinchasi and the 1996 SBOA because the 1996 SBOA teaches that the half-life for Copaxone® is approximately 80 hours in a monkey, which, according to Petitioner and its declarant, is a reliable model for predicting human pharmacokinetic parameters and creating dosing schedules. Pet. 52 (citing Ex. 1007, 197; Ex. 1003, ¶¶ 127, 133, 136–38). Petitioner also notes that the 1996 SBOA questions whether daily injections are necessary and that a reviewer "recommend[ed] that [Teva] evaluate the necessity of daily [subcutaneous] injections as opposed to more infrequent intermittent administration of the drug." Pet. 52 (citing Ex. 1007, 252). Given these teachings of the 1996 SBOA, Petitioner argues that a person of ordinary skill in the art would have understood that the "injection frequencies [of Copaxone®] could be reduced as far as approximately once every 80 hours while maintaining the same safety and tolerability profiles." *Id.* (citing Ex. 1003 ¶¶ 139–41). Accordingly, Petitioner and its declarants assert that a person of ordinary skill in the art would have expected both 40 mg of GA

three times over a seven-day period and 20 mg daily to provide the same therapeutic profile to a patient. *Id.* (citing Ex. 1003 ¶¶ 145–47; Ex. 1004 ¶¶ 103–04).

Petitioner also argues that it would have been obvious to a person of ordinary skill in the art to modify Pinchasi's alternate-day injection schedule to three times in seven days to reduce the number of injections and thereby reduce the frequency of side effects. *Id.* at 46–47 (citing Ex. 1004 ¶¶ 103–04, 109). According to Petitioner, administering the drug three times in seven days would also allow for a more convenient dosing schedule, which would improve patient compliance. *See id.* at 46–47 (citing Ex. 1004 ¶¶ 103–05; Ex. 1003 ¶¶ 107–10).

Patent Owner makes several arguments in response, which we address below. But based on the current record, we conclude that Petitioner has established a reasonable likelihood of prevailing on its assertion that claim 1 is unpatentable as obvious over Pinchasi and 1996 SBOA. We have considered the parties' arguments and evidence with respect to the remaining claims, and we determine that Petitioner has made a sufficient showing as to those claims, as well.[5]

E. Obviousness over Pinchasi and Flechter

Petitioner argues that claims 1–20 of the '413 patent are obvious over Pinchasi and Flechter. Pet. 55–56. Patent Owner opposes. Prelim.

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[5] We recognize that Patent Owner argues that Petitioner "did not set forth any specific argument that the limitations of dependent claims 6 and 14–18 are rendered obvious over the prior art." Prelim. Resp. 51. We disagree. Petitioner argues that the additional limitations of those dependent claims are taught by Pinchasi, and that the claims are obvious over the cited references. Pet. 28–32. Thus, on this record, we find that Petitioner has shown sufficiently that the claims are obvious over the cited references.

Resp. 34–53. Based on the current record, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing claims 1–20 are unpatentable over Pinchasi and Flechter.

1. Flechter (Ex. 1008)

Flechter discloses the results of a multicenter study treating patients with relapsing MS with 20 mg doses of copolymer-1 on alternate days. Ex. 1008, 1.[6] Flechter states that the results of the trial "suggest that alternate-day treatment with Copolymer 1 is safe, well tolerated, and probably as effective as daily Copolymer 1 in reducing relapse rate and slowing neurologic deterioration." *Id.* at 5. Flechter concedes, however, that its study "was uncontrolled," that its conclusions "cannot be used to prove efficacy," and that "these preliminary observations will have to be examined in larger studies." *Id.*

2. Analysis

Petitioner argues that claims 1–20 are unpatentable as obvious over the combination of Pinchasi and Flechter. As above with respect to the 1996 SBOA, Petitioner asserts that Pinchasi teaches each of the limitations of the claims, except the dosing frequency of three injections per week. And, as above, we are persuaded by Petitioner's argument at this stage of the proceeding.

Petitioner then argues that the dosing frequency would have been obvious because a person of ordinary skill in the art would have recognized that the GA dosage from the claimed dosing frequency of three times per

[6] Because the original pagination of Flechter (Ex. 1008) has unique page numbers, it was unnecessary to repaginate the exhibit under 37 C.F.R. § 42.63(d)(2). For purposes of consistency, however, we will continue to cite to the pagination provided by the parties.

week falls within the alternate-day 40 mg dosage regimen of Pinchasi and the alternate-day 20 mg dosage regimen of Flechter. Pet. 55 (citing Ex. 1003 ¶ 154). Petitioner further argues that a person of ordinary skill in the art would have been motivated to set a course of treatment for the same day each week, for example on Monday, Wednesday, and Friday, to increase compliance with the dosage regimen. *Id.* (citing Ex. 1005 ¶¶ 115–16, 18).

Patent Owner makes several arguments in response, which we address below. Based on the current record, however, we conclude that Petitioner has established a reasonable likelihood that it would prevail on its assertion that claim 1is unpatentable as obvious over Pinchasi and Flechter. We have considered the parties' arguments and evidence with respect to the remaining claims, and we determine that Petitioner has made a sufficient showing as to those claims, as well.[7]

F. Patent Owner's Arguments Regarding Obviousness

Patent Owner challenges several aspects of Petitioner's obviousness arguments. For example, Patent Owner argues that a person of ordinary skill in the art would not have had a reasonable expectation of success in using a 40 mg three times per week regimen given GA's complex mechanism of action and the lack of PK/PD correlation. Prelim. Resp. 35–38. Patent Owner also argues that a person of ordinary skill in the art would not have been motivated to dose GA three times per week, particularly when the regimen claimed in the '413 patent "provides 14% less GA to the patient than the approved 20 mg daily dose or Pinchasi's 40 mg, alternate day regimen." *Id.* at 38–44. Moreover, Patent Owner argues that a person of

[7] We address Patent Owner's argument regarding the dependent claims above. *See supra* n.5.

ordinary skill in the art would not have been motivated to use a 40 mg dose of GA in light of other clinical trials that allegedly show a 40 mg daily dose was not superior to a 20 mg daily dose. *Id.* at 45–46. Finally, Patent Owner argues that there was no reason to combine Pinchasi with the 1996 SBOA or Flechter, and that secondary considerations support a finding of nonobviousness of the claims. *Id.* at 46–48, 54–58.

Although Patent Owner's arguments are compelling, they generally amount to a difference in opinion as to the evidence set forth by Petitioner. At this stage of the proceeding, we find that Petitioner has offered sufficient evidence to institute trial. That being said, we will be able to evaluate both parties' arguments more thoroughly once the record is developed further during trial.

G. Remaining Challenge

Petitioner also asserts that claims 1–20 are unpatentable as obvious over Pinchasi alone. Pet. 20–45. In light of our findings above with respect to Pinchasi, the 1996 SBOA, and Flechter, we exercise our discretion not to institute an *inter partes* review on this ground. *See* 37 C.F.R. § 42.108(a).

III. CONCLUSION

We conclude that Petitioner has established a reasonable likelihood of prevailing on its assertions that claims 1–20 of the '413 patent are unpatentable as obvious.

At this stage of the proceeding, the Board has not made a final determination as to the patentability of any challenged claim or the construction of any claim term.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes*

review is hereby instituted on the following grounds:

A. Claims 1–20 as obvious over Pinchasi and 1996 SBOA; and

B. Claims 1–20 as obvious over Pinchasi and Flechter.

FURTHER ORDERED that no other proposed grounds of unpatentability are authorized.

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this decision.

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