UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ERWIN SCHOLLMAYER[1]

Appeal 2014-004849
Application 10/429,283
Technology Center 1600

Before CHRISTOPHER G. PAULRAJ, JACQUELINE T. HARLOW, and DAVID COTTA, *Administrative Patent Judges*.

HARLOW, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method for the treatment of restless leg syndrome. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] According to Appellant, the Real Party in Interest is UCB Pharma GmbH (App. Br. 3).

STATEMENT OF THE CASE

The "invention relates to the use of rotigotine for the effective treatment of Restless Leg Syndrome (RLS)." Abstract.

Claims 1, 3, 27, 29, 35, and 37–45 are on appeal. Claim 1 is illustrative and reads as follows:

> 1. A method of long-term dopamine agonist therapy for a subject suffering from Restless Leg Syndrome (RLS), the method comprising transepicutaneously administering to the subject rotigotine in a daily dosage amount of 0.5 to 10 mg effective to provide in at least 8 days an improvement of about 2 or more units on the International Restless Leg Syndrome Study Group (IRLSSG) scale, as compared to a placebo treatment.

The claims stand rejected as follows:

Claims 1, 3, 27, 29, 35, and 37–44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Rimpler[2] and Muller.[3]

Claim 45 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Rimpler, Muller, Brecht,[4] and Horowski.[5]

I.

The Examiner has rejected claims 1, 3, 27, 29, 35, and 37–44 under 35 U.S.C. § 103(a) as being unpatentable over Rimpler and Muller. We focus our discussion on claim 1, which is representative. We also address claims 37 and 41–44, as these claims are separately argued.

The Examiner finds that Rimpler discloses rotigotine as "a potent and selective D2 agonist that plays a significant role in the treatment of

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[2] Rimpler et al., US 2003/0166709 A1, published Sep. 4, 2003.
[3] Muller et al., WO 99/49852, published Oct. 7, 1999. Citations to English equivalent, US 6,884,434 B1, issued Apr. 26, 2005.
[4] Brecht, US 2001/0053777 A1, published Dec. 20, 2001.
[5] Horowski et al., US 2004/0028723 A1, published Feb. 12, 2004.

dopamine-related disorders such as Parkinson's disease and Restless Leg." Ans. 2. The Examiner also finds that Rimpler discloses that transdermal systems have been developed for the delivery of rotigotine to a patient. *Id.* The Examiner finds that Rimpler teaches that rotigotine treatment may be administered in the form of monotherapy, or in combination with other antiparkisonian agents. *Id.*

The Examiner acknowledges that Rimpler does not specifically identify the ingredients of transdermal rotigotine treatment systems, but finds that Muller cures this deficiency. *Id.* at 3. In particular, the Examiner finds that Muller discloses transdermal administration of 10 mg of rotigotine in a 20 cm^2 patch, which corresponds to 0.5 mg/cm^2. *Id.* The Examiner further finds that Muller teaches a daily dosage range of 1–20 mg, and a plaster size range of 2–40 cm^2, and that the matrix of the transdermal system can be an acrylate-based or silicone-based polymer adhesive system. *Id.*

The Examiner finds that an ordinarily skilled artisan would have "been motivated to utilize the transdermal patch system of Muller et al. in the treatment of Restless Leg Syndrome because Rimpler et al. teach that N-0923 (rotigotine) is known to treat Parkinson's Disease and Restless Leg and that this compound has been formulated into transdermal patch form." *Id.* at 3–4.

We agree with the Examiner that the combination of Rimpler and Muller renders obvious claims 1, 37, and 41–44, and adopt the Examiner's findings concerning the scope and content of the prior art. We address Appellants' arguments below.

Claim 1

We do not find persuasive Appellants' contention, set forth in the Appeal Brief, that an ordinarily skilled artisan in possession of Rimpler and Muller would not have had reason to use a rotigotine patch to treat RLS because those references "fail to teach or suggest the claimed Rotigotine Administration Route, [and] the entire field of RLS treatment fails to motivate one of ordinary skill in the art to utilize a patch system to treat RLS" (App. Br. 8).

As an initial matter, we note that during oral argument Appellants clarified that they do not dispute that the combination of Rimpler and Muller discloses the treatment of RLS with a rotigotine patch. Hearing Trans. 6:3–7 ("JUDGE HARLOW: . . . . So you're not disputing that the combination of Rimpler and Muller would disclose the treatment of RLS with a rotigotine patch. Is that correct? MS. KORAL: I'm not disputing it based on what our current claim language is."). For completeness, we additionally observe that Rimpler discloses that rotigotine "is a potent and selective dopamine D2 agonist playing a signification role in the treatment of all diseases associated with a dopamine-related metabolic disorder such as . . . Restless Leg" (Rimpler ¶ 4), and explains that "transdermal systems" for rotigotine administration have been developed in an attempt to address the shortcomings of oral delivery (Rimpler ¶¶ 9–10). Indeed, Rimpler identifies Muller as a known transdermal patch for rotigotine administration. *Id.* ¶ 9. Accordingly, we agree with the Examiner that an ordinarily skilled artisan in possession of Rimpler and Muller would have had reason to use the rotigotine patch of Muller to treat RLS. Ans. 3–4.

Appellants' contention that the cited combination fails to disclose the claimed "dosage window" (App. Br. 8–9) is similarly unavailing. The daily dosage range of 0.5–10 mg recited in claim 1 is prima facie obvious in view of Muller's disclosure of administering 1–10 mg of rotigotine daily (Muller 4:9–17). *See In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003) ("In cases involving overlapping ranges, we and our predecessor court have consistently held that even a slight overlap in range establishes a prima facie case of obviousness."); *In re Aller*, 220 F.2d 454, 456 (CCPA 1955) ("[I]it is not inventive to discover the optimum or workable ranges by routine experimentation.").

Furthermore, we agree with the Examiner that because Muller teaches the composition, dosage form, and dosage required by the claimed invention, in the absence of any contrary showing by Appellants, there is a reasonable basis to conclude that the properties of the claimed invention are inherent in the composition of Muller. Ans. 11; *see also PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1196 (Fed. Cir. 2014) (explaining that in an obviousness analysis inherency is appropriately relied upon to establish the existence of a claim limitation where the limitation at issue is necessarily present, "or the natural result of the combination of elements explicitly disclosed by the prior art"); *In re Papesch*, 315 F.2d 381, 391 (CCPA 1963) (a chemical compound and its properties are inseparable); *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990) ("when the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.").

Appellants' reliance on the Federal Circuit's decisions in *Allergan Inc. v. Sandoz Inc.*, 726 F.3d 1286 (Fed. Cir. 2013), and *Pozen Inc. v. PAR*

Pharm., Inc., 696 F.3d. 1151, 1165 (Fed. Cir. 2012) (App. Br. 9–10), does not dictate a different result. Neither *Allergan* nor *Pozen* involved a situation where the claimed composition was expressly disclosed by the prior art; nor did the court in those cases address a dispute as to whether a claimed benefit of a disclosed compound was an inherent property of the compound. *Allergan Inc.*, 726 F.3d at 1290; *Pozen Inc.*, 696 F.3d. at 1161–1165. Indeed, in *Allergan*, no allegation was made that the disputed limitation was inherent to the composition claimed (726 F.3d at 1294), and the portion of *Pozen* relied upon by Appellants does not concern inherency, but rather, existence of a motivation to combine two prior art compounds (696 F.3d. at 1165).

We are also unpersuaded by Appellants' contention that an ordinarily skilled artisan would not have had a reasonable expectation of success in performing the claimed method (*see* App. Br. 10–13). As explained above, Rimpler teaches the use of rotigotine to treat RLS, and identifies Muller as a known prior art patch for transdermal rotigotine administration. Rimpler ¶¶ 4, 9. The patch disclosed by Muller is described as providing a daily dose of 1–10 mg of rotigotine. Muller, 4:9–17. We thus agree with the Examiner that "[s]ince a patch known to transepicutaneously deliver rotigotine delivers the drug in the same amount as instantly claimed, the active method steps are suggested by the prior art." Ans. 14. *See KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) ("If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability."); *see also id.* at 420 ("[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed."); *In re Baxter-Travenol Labs.*, 952

F.2d 388,392 (Fed. Cir. 1991) ("Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention.").

We recognize Appellants' contention that it would not have been obvious to try various dopamine agonists in order to arrive at the claimed invention. App. Br. 12–13. We note, however, that this argument is moot in view of the explicit disclosures of Rimpler and Muller.

Turning to Appellants assertion that the relevant art is unpredictable, and the claimed method yields unexpected results, we observe that neither Table 1 of the Appeal Brief, which compiles the results of studies assessing the augmentation profiles observed with various dopamine agonists, nor the Schollmayer Declaration, which includes data similar to Table 1, as well as clinical trial results comparing the claimed RLS treatment to placebo, establishes that the art is unpredictable, or that the results obtained from performing the claimed method are unexpected.

As an initial matter, as the Examiner observes, Appellants do not present a side-by-side comparison of RLS treatment results obtained via the claimed method and the closest prior art. Ans. 14–15. For example, Table 1 of the Appeal Brief compares results obtained from rotigotine patch treatment with those obtained from peroral treatment with other dopamine agonists. Notably, Table 1 aggregates data from different sources, collected using different protocols, and does not represent a true side-by-side comparison of experimental results. In addition, Appellants do not provide data from treatment with prior art dopamine agonist patches, such as lisuride patches, or prior art rotigotine dosage forms, such as the depot dosage form disclosed by Rimpler (Rimpler ¶ 26). Thus, neither Table 1 nor the

Schollmayer Declaration can be said to represent a comparison of the claimed invention with the closest prior art.

Furthermore, Appellants do not establish that the allegedly improved results observed with a rotigotine patch as compared to oral forms of pramipexole and ropinerole are unexpected. Rather, we agree with the Examiner that an ordinarily skilled artisan would have expected increased bioavailability and reduced side effects from transdermal administration of dopamine agonists, as compared to peroral administration. Ans. 15. In this regard, we observe that Rimpler discloses that peroral administration of rotigotine is therapeutically ineffective due to poor bioavailability, and observes that other dosage forms, including transdermal patches, have been developed to overcome the shortcomings of peroral administration (Rimpler ¶¶ 4, 8, 9). We also agree with the Examiner that Horowski, which is prior art to the claimed invention (and cited in the rejection of claim 45), evidences that an ordinarily skilled would have expected improved RLS treatment outcomes from transdermal dopamine agonist dosage forms as compared to peroral administration. Ans. 14–15; *see also* Horowski ¶¶ 1–6 ("Bioavailability is increased by the TTS as compared to peroral administration, which typically reduces the overall dose required to achieve the therapeutically desirable effect.").

Claims 37 and 44

Claim 37 depends from claim 1 and further recites "wherein the administration is in monotherapy." Independent claim 44 recites "[a] method of treating RLS, the method comprising transepicutaneously administering to the subject rotigotine in a daily dosage amount of 0.5 to 5 mg, wherein the administration of rotigotine is in monotherapy."

Appellants argue that claims 37 and 44 are nonobvious because Rimpler "fails to disclose the treatment of RLS by transepicutaneously administering rotigotine in monotherapy" and "M[u]ller is directed to the treatment of Parkinson's disease." App. Br. 15, 18.

As explained above with regard to claim 1, an ordinarily skilled artisan in possession of the cited references would have had reason to use the transdermal patch of Muller to treat RLS, as taught by Rimpler. Furthermore, Rimpler expressly discloses the use of rotigotine monotherapy to treat RLS (Rimpler ¶ 20). In addition, for the reasons discussed above with regard to claim 1, we determine that the daily dosage range of 0.5–5 mg recited in claim 44 is prima facie obvious in view of Muller's disclosure of administering 1–20 mg of rotigotine daily (Muller 4:9–17). *See In re Peterson*, 315 F.3d at 1329; *In re Aller*, 220 F.2d at 456. Accordingly, we agree with the Examiner that claims 37 and 44 are prima facie obvious in view of Rimpler and Muller. *See In re Merck & Co., Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986) ("Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. . . . [The reference] must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole.").

We further agree with the Examiner, contrary to Appellants' intimation (App. Br. 16, 18–19), that Brecht, which is not relied upon in the rejection of claim 37 or claim 44, does not teach away from rotigotine monotherapy. Ans. 15. *See In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994) ("A known or obvious composition does not become patentable simply

because it has been described as somewhat inferior to some other product for the same use.").

Claims 41 and 42

Claim 41 depends from claim 1, and further recites "wherein the subject is augmentation-prone, but wherein augmentation during said long-term therapy is suppressed." Independent claim 42 recites:

> 42. In a method using a dopamine agonist for long-term therapy for a subject suffering from RLS, said subject being augmentation-prone under long-term dopamine agonist therapy, the improvement comprising
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> transepicutaneously administering rotigotine to the subject in a daily dosage amount of 0.5 to 10 mg effective to provide in at least 8 days an improvement of about 2 or more units on the IRLSSG scale, as compared to a placebo treatment.

Appellants assert that because "[a] patient who is augmentation prone is even more likely to experience augmentation," "rotigotine's reduction of the [augmentation]-profile for such patient population is even further unpredictable to one of ordinary skill in the art." App. Br. 17.

We do not agree. As explained above with regard to claim 1, Appellants have not established either that the relevant art was unpredictable, or that the results obtained in performing the claimed method were unexpected. Furthermore, we agree with the Examiner that it would have been obvious to an ordinarily skilled artisan, based on Rimpler's disclosures concerning the usefulness of rotigotine to treat RLS, to administer rotigotine to RLS patients who previously suffered from augmentation. Ans. 15–16.

Claim 43

Independent claim 43 recites:

> 43. A method of treating RLS in a subject at least 40 years old, the method comprising
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> transepicutaneously administering to the subject rotigotine in a daily dosage amount of 0.5 to 10 mg effective to provide in at least 8 days an improvement of about 2 or more units on the IRLSSG scale, as compared to a placebo treatment.

Claim 43 closely mirrors claim 1, but additionally recites that the subject treated is at least 40 years old. Appellants acknowledge that Muller discloses that Parkinson's disease typically sets in between 58 and 62 years of age, but contend that it would not have been obvious to treat RLS sufferers of at least 40 years old according to the claimed method based on the teachings of Rimpler and Muller. App. Br. 17–18.

We do not agree. As explained above, Rimpler and Muller render obvious the treatment of RLS patients with the rotigotine patch of Muller, including those of at least 40 years in age.

Conclusion

For the reasons set forth above, we conclude that a preponderance of the evidence of record supports the Examiner's conclusion that the combination of Rimpler and Muller renders claims 1, 37, and 41–44 obvious. Claims 3, 27, 29, 35, and 38–40 have not been argued separately and therefore fall with claim 1.

II.

The Examiner has rejected claim 45 under 35 U.S.C. § 103(a) as being unpatentable over Rimpler, Muller, Brecht, and Horowski.

Claim 45 recites:

> 45. A method of treating RLS in a patient who is experiencing augmentation or who has experienced augmentation, the method comprising
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> transepicutaneously administering to the subject rotigotine in a daily dosage amount of 0.5 to 10 mg effective to provide in at least 8 days an improvement of about 2 or more units on the IRLSSG scale, as compared to a placebo treatment.

The Examiner reiterates the findings and conclusions set forth above with regard to claim 1 concerning the combination of Rimpler and Muller.

The Examiner additionally finds that Brecht teaches transdermal administration of dopamine agonists to treat RLS, and discloses that "administration of L-DOPA led to typical augmentation during the day but this augmentation disappeared when the patients switched to the dopamine agonist." Ans. 7.

The Examiner finds that Horowski describes a transdermal therapeutic system for treating RLS. *Id.* The Examiner finds that Horowski discloses that peroral dopaminergic therapies often lead to rebound and augmentation, while transdermal therapies prevent these side effects. *Id.*

In addition to the reasons to combine Rimpler and Muller set forth above with respect to claim 1, the Examiner finds that "[o]ne of ordinary skill in the art would have been motivated to utilize [Muller's] patch in a patient who previously had augmentation as Brecht teaches that administration of L-DOPA led to typical augmentation during the day but this augmentation disappeared when the patients switched to the dopamine agonist." *Id.* at 8. The Examiner further concludes that "based on the

teachings of Brecht and Horowski et al. one of ordinary skill in the art would have a reasonable expectation that administration of N-0923 [rotigotine] would additionally lead to disappearance of augmentation as compared to L-DOPA administration when delivered via a transdermal patch." *Id.* at 9.

We agree with the Examiner that the combination of Rimpler, Muller, Brecht, and Horowski renders obvious claim 45, and adopt the Examiner's findings concerning the scope and content of the prior art. We address Appellants' arguments below.

Appellants contend that Brecht does not teach or suggest that rotigotine doses resulting in a two-unit improvement on the IRLSSG scale could also reduce the augmentation-profile for patients experiencing, or who have experienced, augmentation. App. Br. 20. Appellants similarly assert that an ordinarily skilled artisan would not have predicted, and that there is no suggestion of an expectation of success, that transdermal administration of rotigotine could reduce clinically-significant augmentation while maintaining an improvement of at least two units on the IRLSSG scale. *Id.* Appellants also argue that Brecht "seems to discourage only using DAs as a treatment for RLS as evidenced by the undesirable side effects associated with their use, especially if the dosage needs to be increased." *Id.*

We are not persuaded. As an initial matter, we note that claim 45 requires only that a patient who is experiencing, or who *has experienced* augmentation achieve an improvement of about two or more units on the IRLSSG scale, relative to placebo, with transepicutaneous rotigotine treatment. Claim 45 states no additional requirement that the recited method produce a reduced augmentation-profile for patients; neither does claim 45 require monotherapy. Accordingly, we decline to read such limitations into

that claim. *See Bayer AG v. Biovail Corp.*, 279 F.3d 1340, 1348, (Fed. Cir. 2002) ("[A] court may not read into a claim a limitation from a preferred embodiment, if that limitation is not present in the claim itself.").

Moreover, we agree with the Examiner that one of ordinary skill in the art would have had reason to combine Rimpler, Muller, Brecht, and Horowski, and further, had a reasonable expectation of success that transdermal rotigotine administration to patients experiencing, or who have experienced augmentation, would result in a reduction in augmentation relative to other therapies. Ans. 9. In particular, we agree with the Examiner that

> based on the teachings of Brecht it is known that administration of L-DOPA can lead to augmentation, however, Brecht additionally teaches that this augmentation disappeared when the patient switched to a dopamine agonist. Horowski et al. teaches that transdermal therapy affords many benefits over peroral administration such that a continuous active ingredient flux is established so that plasma concentrations can be set as defined and variations can be controlled and decomposition in the plasma is fast and controlled. This allows for prevention of the side effects associated with peroral administration which includes augmentation. Therefore, based on the teachings of Brecht and Horowski et al. one of ordinary skill in the art would have a reasonable expectation that administration of N-0923 [rotigotine] would additionally lead to disappearance of augmentation as compared to L-DOPA administration when delivered via a transdermal patch.

Id.

Turning to Appellants' contention that the purportedly unexpected results obtained from transdermal treatment of RLS patients with rotigotine are sufficient to rebut the Examiner's showing of prima facie obviousness, as explained above with regard to claim 1, we determine that Appellants have not established that alleged improvements observed with transdermal

rotigotine treatment were in fact unexpected. We agree with the Examiner that based on the teachings of Brecht, "one of ordinary skill in the art would expect that when you switch from L-DOPA to another dopamine agonist you would expect a decrease in the degree of augmentation," and that "it is reasonable to expect that there would be a difference in degree in the reduction in the augmentation when switching from one dopamine agonist to another." Ans. 13. Moreover, as detailed above, the data Appellants present is not a side-by-side comparison with the closest prior art.

Accordingly, for the reasons set forth above, we conclude that a preponderance of the evidence of record supports the Examiner's conclusion that the combination of Rimpler, Muller, Brecht, and Horowski renders claim 45 obvious.

SUMMARY

We affirm the rejection of claims 1, 37, and 41–44 under 35 U.S.C. § 103(a) based on Rimpler and Muller. Claims 3, 27, 29, 35, and 38–40 fall with claim 1.

We affirm the rejection of claim 45 under 35 U.S.C. § 103(a) based on Rimpler, Muller, Brecht, and Horowski.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED