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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte RICHARD JAMES CAWTHRAY,
VINCENT ANTHONY DiFABRITUS, ELLEN MARY LOUGHREN,
KURT FRANKLIN TROMBLEY, and
STEPHANUS ALEXANDER PAULUS VAN DER GEEST¹

Appeal 2015-006663
Application 13/325,170
Technology Center 1600

Before RICHARD M. LEBOVITZ, JOHN G. NEW, and
TIMOTHY G. MAJORS, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

DECISION ON APPEAL

¹Appellants state the real party-in-interest is Warner Chilcott Company, LLC. App. Br. 1.

SUMMARY

Appellants file this appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 24, 26, 29 and 34 as unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of Daifotis et al. (US 5,994,329, November 30, 1999) ("Daifotis"), Kelly (US 4,817,819, April 4, 1989) ("Kelly"), Mazel et al. (US 2001/0044427 A1, November 22, 2001) ("Mazel"), and Hendricks (US 2003/0031726 A1, February 13, 2003) ("Hendricks").²

We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

NATURE OF THE CLAIMED INVENTION

Appellants' invention is directed to a kit for promoting the proper sequential oral administration of a pharmaceutically active ingredient and accompanying nutrients in a blister card. The claims at issue in this appeal are drawn to a method for increasing compliance for a treatment regimen comprising providing the kit to a person in need of treatment. Abstract.

REPRESENTATIVE CLAIM

Appellants argue all of the claims together. App. Br. 3. Claims 24 is representative of the claims on appeal and recites:

24. A method for increasing compliance with a treatment regimen for treating or preventing osteoporosis comprising providing a person in need thereof a kit for sequential and continuous oral administration of a bisphosphonate and an accompanying nutrient, said kit comprising:

² Claims 1–23, 25, 27, 28, 30–33, and 35 are cancelled. App. Br. 1.

(a) at least one unit dose of the bisphosphonate to be given continuously on a frequency of once a week, wherein the bisphosphonate is selected from the group consisting of risedronate and pharmaceutically acceptable salts thereof, and wherein each unit dose is 35 mg of the bisphosphonate;

(b) at least one unit dose of a nutrient to be given subsequent to the active dose administration, wherein the nutrient is selected from the group consisting of calcium, calcium and vitamin D, and a combined unit dose of calcium and vitamin D, and wherein the unit doses of calcium are about 400 mg to about 1500 mg of elemental calcium per day and the unit doses of vitamin D are about 100 IU to 10,000 IU per day; and

(c) a blister card individually and releasably containing the unit doses;

wherein said unit doses of the bisphosphonate and nutrient are arranged horizontally or vertically in order of their use across the blister card, and

wherein the kit provides instructions to the person using the kit to avoid the simultaneous daily dosing of the bisphosphonate and the nutrient.

App. Br. 11.

ISSUES AND ANALYSIS

We adopt the Examiner's findings and conclusions that Appellants' claim is *prima facie* obvious over the combined cited prior art. We address below the arguments raised by Appellants on appeal.

Issue

Appellants argue the Examiner erred in finding that the combined cited prior art teaches or suggests all of the limitations of claim 24. App. Br. 3.

Analysis

1. Daifotis

The Examiner finds Daifotis teaches a method of inhibiting bone resorption by administering a bisphosphonate once a week, where the bisphosphonates include alendronate and risedronate. Final Act. 2–3 (citing Daifotis col. 6, ll. 43–50). The Examiner finds Daifotis teaches the administration periods may last from 1 month to about 20 years. *Id.* at 3–4 (citing Daifotis col. 7, ll. 61–67). The Examiner finds Daifotis teaches kits, including a card with the dosages oriented in the order of their intended use. *Id.* at 4. An example of such a kit is a blister pack, which is well-known in the art of dosaging. *Id.* at 3.

Appellants argue Daifotis fails to teach or suggest a blister pack “as disclosed in the present invention,” and further fails to teach or suggest any regimens administering doses of a calcium-containing nutrient. App. Br. 6. Appellants argue further that Daifotis neither teaches nor suggests 35 mg unit doses of risedronate, as required by the claims on appeal. *Id.*

Appellants argue further that Daifotis neither teaches nor suggests a dual component treatment of administering calcium and a bisphosphonate, or the problem associated with administering calcium concurrently with a bisphosphonate, and, therefore, does not render obvious a solution for

increasing compliance with such a treatment by avoiding simultaneous dosing, i.e., taking a bisphosphonate on a different day than a calcium-containing nutrient. App. Br. 6. Appellants assert Daifotis lists possible additional dosages to the kit, including calcium, as a potential memory aid, however, it does not specify that adding calcium-containing nutrients is a part of the very treatment itself and use of a kit would increase compliance with a specific and potentially confusing treatment regimen. *Id.*

Appellants argue further that Daifotis does not teach or suggest a calcium-containing nutrient should be taken subsequent to the active dosage for treatment and health benefits. App. Br. 6. Rather, Appellants contend, Daifotis states that placebo dosages, or calcium or dietary supplements, can be included to provide for a kit in which a dosage is taken every day. *Id.* at 6–7. Appellants assert it would not be obvious to an ordinary artisan reading Daifotis to choose a calcium-containing nutrient over the potentially hundreds of other options found within the Daifotis’ “placebo dosages, or calcium or dietary supplements,” or to take the calcium-containing nutrient subsequent to and in between the days when taking the active compound. *Id.* at 7.

The Examiner responds that Daifotis was not relied upon to teach the recited dosages of calcium and vitamin D; nor was Daifotis relied upon to teach the claimed dosage of risedronate. Ans. 5. Rather, the Examiner relies upon Daifotis as teaching the administration of risedronate and calcium in blister packs, for the inhibition of bone resorption. *Id.*

The Examiner also finds Daifotis teaches effectively administering bisphosphonate to a patient, and that Daifotis further suggests using a nutrient such as calcium on the days that the bisphosphonate is not taken.

Ans. 6. The Examiner therefore finds that a person of ordinary skill in the art would realize Daifotis teaches administration of a bisphosphonate and a calcium nutrient concurrently on different days. *Id.* The Examiner finds that calcium, which is either in a form similar to or distinct from the bisphosphonate dosages, is included in the kit, where dosages are taken every day (e.g., to act as a memory aid), consequently, the patient will not miss a dose of bisphosphonate. *Id.* The Examiner further, finds that, simply because Daifotis discloses a multitude of placebo drugs, this does not necessarily render any particular formulation less obvious. *Id.* (citing *Merck & Co., Inc. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989).

The Examiner's findings are supported by a preponderance of the evidence. Daifotis teaches:

The methods of the present invention comprise orally administering to a mammal a pharmaceutically effective amount of a bisphosphonate as a unit dosage, wherein said dosage is administered according to a continuous schedule having a dosing interval selected from the group consisting of once-weekly dosing, twice-weekly dosing, 50 biweekly dosing, and twice-monthly dosing.

Daifotis col. 6, ll. 45–50. Daifotis also teaches:

In further embodiments, the present invention relates to a kit for conveniently and effectively carrying out the methods in accordance with the present invention. Such kits are especially suited for the delivery of solid oral forms such as tablets or capsules. Such a kit preferably includes a number of unit dosages. Such kits can include a card having the dosages oriented in the order of their intended use. An example of such a kit is a “blister pack”. Blister packs are well known in the packaging industry and are widely used for packaging pharmaceutical unit dosage forms. If desired, a memory aid can be provided, for example in the form of numbers, letters, or other

markings or with a calendar insert, designating the days in the treatment schedule in which the dosages can be administered. *Alternatively, placebo dosages, or calcium or dietary supplements, either in a form similar to or distinct from the bisphosphonate dosages, can be included to provide a kit in which a dosage is taken every day.*

Daifotis col. 13, ll. 48–65 (emphasis added).

Daifotis thus teaches the weekly administration of bisphosphonate, with the dosages presented in a blister card, the weekly dosages of bisphosphonate interspersed in the blister card between calcium supplements, as recited in claim 24. We therefore find Daifotis teaches the elements of claim 24 cited by the Examiner. Moreover, we disagree with Appellants that a person of ordinary skill would not choose a calcium-containing nutrient over the potentially hundreds of other options found within the Daifotis’ “placebo dosages, or calcium or dietary supplements,” or to take the calcium-containing nutrient subsequent to and between the days when taking the bisphosphonate, because, as quoted above, this is the plain teaching of Daifotis.

With respect to Appellants’ remaining arguments, the Examiner did not rely upon Daifotis as teaching those limitations argued by Appellants. “[O]ne cannot show non-obviousness by attacking references individually where ... the rejections are based on combinations of references.” *In re Keller*, 642 F.2d 413, 426 (C.C.P.A. 1981).

2. *Kelly*

Appellants argue *Kelly* neither teaches nor suggests a blister pack containing risedronate in 35 mg unit doses and a calcium-containing nutrient

as a treatment regimen or for increasing compliance with a treatment or prevention regimen, such that the active is taken on different days than the calcium-containing nutrient, thereby ensuring availability of calcium for bone matrix mineralization, calcium homeostasis and avoidance of secondary hyperparathyroidism, while avoiding a reduction in the benefits of the treatment due to simultaneous administration. App. Br. 7.

Appellants also contend Kelly fails to teach or suggest administration of unit doses of an accompanying calcium-containing nutrient, or that the unit doses of calcium of about 400 mg to about 1500 mg of elemental calcium per day and unit doses of vitamin D are about 100 IU to 10,000 IU per day. App. Br. 7. Rather, Appellants assert Kelly teaches only that seven tablets in the blister pack might be a placebo or non-active tablet and the purpose of the blister packs is generally to act as memory aids. *Id.* at 7–8.

The Examiner responds that Kelly was not relied upon to teach increased compliance with a blister pack, rather that it is the combination of Daifotis and Mazel that teaches increased compliance. Ans. 6–7.

Appellants' arguments are not persuasive because the Examiner did not rely on Kelly for teaching the dosages of calcium or risedronate. Rather, the Examiner relied upon Mazel and Hendricks for these teachings. Final Act. 4. Appellants cannot successfully allege that the reference teaches limitations other than those the Examiner relies upon the reference as teaching. *See Keller*, 642 F.2d at 426.

3. *Mazel and Hendricks*

The Examiner relies on Mazel as teaching risedronate tablets (35 mg) to treat or prevent osteoporosis. Final Act. 4 (citing Mazel ¶¶ 12; 158). The Examiner finds Mazel teaches risedronate is administered as once weekly dosages by blister pack, which serves as a memory aid and is useful for improving patient acceptance and compliance. *Id.* (citing Mazel ¶¶ 9, 38 42; 151; 157–158).

The Examiner finds Hendricks teaches tablets comprising calcium and vitamin D for the improvement of bone health and for the prevention of osteoporosis. Final Act. 4 (citing Hendricks Abstr.; ¶ 15). The Examiner finds Hendricks teaches calcium (1000 mg) and Vitamin D (400 IU) presented in a combined tablet administered as a daily dosage formulation. *Id.* (citing Hendricks ¶¶ 15; 41).

Appellants argue Mazel and Hendricks fail to remedy the deficiencies of Daifotis and Kelly, because there is no teaching or suggestion of a blister pack containing a multi-component treatment of bisphosphonate and a calcium-containing nutrient for increasing compliance with a treatment or prevention regimen, such that the active is taken on different days than the calcium containing nutrient, thereby ensuring availability of calcium for bone matrix mineralization, calcium homeostasis and avoidance of secondary hyperparathyroidism, and improving the benefits of the treatment by avoiding simultaneous administration. Appeal Br. 8.

As an initial matter, Appellants' argument that the references fail to teach or suggest "thereby ensuring availability of calcium for bone matrix mineralization, calcium homeostasis and avoidance of secondary hyperparathyroidism, and improving the benefits of the treatment by

avoiding simultaneous administration” is not persuasive. App. Br. 8. To the extent this advantage is a result of step (b) of the claim in which calcium and vitamin D is administered, the Examiner provided adequate evidence, as explained in more detail below, that this step would have been obvious to one of ordinary skill in the art.

Mazel is directed to “provid[ing] such kits and methods for inhibiting bone resorption and for treating or preventing disease states involving bone resorption, such as osteoporosis.” Mazel ¶ 12. Specifically, Mazel teaches: “Examples of such tablets include tablets containing about 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, or 50 mg of a risedronate compound, particularly risedronate monosodium hemi-pentahydrate, on an acid, i.e.[,] risedronic acid, active basis.” *Id.* ¶ 158. These are the passages the Examiner relied upon as teaching the limitation of claim 24 reciting: “wherein the bisphosphonate is selected from the group consisting of risedronate and pharmaceutically acceptable salts thereof, and wherein each unit dose is 35 mg of the bisphosphonate.”

Hendricks is directed to: “A dietary supplement composition contains phosphorus and from greater than 1.3 to less than 2.2 parts by weight calcium per part by weight phosphorus, and may, optionally, further contain Vitamin D.” Hendricks Abstr. Specifically, Hendricks teaches: “The 808 mg tablets contained about 1000 mg calcium, 583 mg phosphorus, 400 IU Vitamin D, 15 mg Vitamin B₆, 1000 mcg folic acid and 500 mcg Vitamin B₁₂ per 4 tablets.” *Id.* ¶ 41. The Examiner relies upon these passages of Hendricks as teaching the limitation of claim 24 of step (b) reciting:

[W]herein the nutrient is selected from the group consisting of calcium, calcium and vitamin D, and a combined unit dose of calcium and vitamin D, and wherein the unit doses of calcium are about 400 mg to about 1500 mg of elemental calcium per day and the unit doses of vitamin D are about 100 IU to 10,000 IU per day.

We agree with the Examiner that the cited passages of Mazel and Hendricks teach the limitations in question.

Appellants persist in arguing the references individually, rather than what the combined references would have suggested to a person of ordinary skill in the contemporaneous art. However:

The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art.

Keller, 642 F.2d at 425. We agree with the Examiner's findings, as related *supra*, that the cited references teach or suggest all of the limitations of the claims on appeal.

Furthermore, a preponderance of the evidence supports the Examiner's conclusion that it would have been obvious to one of ordinary skill in the art to have used a blister pack with four rows, and with seven spaces each, as taught by Kelly and Daifotis, and that an ordinary artisan would be motivated by the desire to use a blister pack and container that is labeled with the day therapy begins, suitable for use for storing pills that are to be taken once a day. Final Act. 4.

Moreover, a preponderance of the evidence supports the Examiner's conclusion that, because Daifotis teaches bisphosphonate for inhibiting bone resorption, it would have been obvious to one of ordinary skill in the art to modify the method of Daifotis by substituting risedronate (which is a bisphosphonate) at 35 mg because Mazel teaches it is useful and convenient for preventing osteoporosis, and further teaches it is useful for improving patient acceptance and compliance. *Id.*

Finally, a preponderance of the evidence supports the Examiner's conclusion that, because Daifotis teaches a method of inhibiting bone resorption, it would have been obvious to one of ordinary skill in the art to modify the method of Daifotis with calcium and vitamin D at the claimed dosages, because tablets comprising calcium at 1000 mg and Vitamin D at 400 IU in a combined dose are useful for bone health and the prevention of osteoporosis, as taught by Hendricks. As indicated above, any advantages of the combination would be a consequence of following the teachings in Hendricks as to the presence and amounts of calcium and vitamin D.

4. The Declaration of Dr. Stefan van der Geest

Appellants next point to the Declaration of Dr. Stefan van der Geest (the "Geest Declaration"), one of the inventors of the instant application. Geest Decl. ¶ 3. According to Appellants, the Geest Declaration demonstrates that correct administration of bisphosphonates is essential to successful treatment of osteoporosis. App. Br. 9. Appellants contend the method of the presently claimed invention not only improves compliance, but also improves the outcomes of treatment and prevention. *Id.* Appellants contend the art cited by the Examiner fails to either teach or suggest the

importance of increasing compliance in correct dosing of a bisphosphonate and a calcium-containing nutrient to avoid simultaneous daily dosing and gain the health and medical advantages achieved by using the method of the present invention. *Id.*

The Examiner agrees that the study cited in the Geest Declaration demonstrates that the claimed blister pack of Appellants' invention increases patient understanding, when compared with blister packs without instructions. Ans. 10. However, the Examiner finds Daifotis, Kelly, and Mazel all each teach blister packs with instructions or memory aids. *Id.* Therefore, the Examiner concludes, Appellants' evidence is not considered to show an unexpected improvement as compared with the prior art, as memory aids would be expected to aid patient understanding and compliance. *Id.*

We agree with the Examiner. The Geest Declaration states:

The combination pack was preferred by the participants, over the same medication from separate packs. Participants better understood the dosing instructions of the combination pack and patients are, therefore, more likely to comply with the instructions and benefit from treatment.

Our results indicate that the combination pack is perceived to simplify a complex therapy regime. Several authors have stated that simplification of therapy enhances adherence. Thus, simplification of therapy of a combined pack of risedronate and calcium-containing supplement is expected to lead to improved compliance and adherence to treatment

Geest Decl. ¶ 13. However, Daifotis teaches:

If desired a memory aid can be provided, for example in the form of numbers, letters, or other markings or with a calendar insert, designating the days in the treatment schedule in which the

dosages can be administered. Alternatively, placebo dosages, or calcium or dietary supplements, either in a form similar to or distinct from the bisphosphonate dosages, can be included to provide a kit in which a dosage is taken every day.

Daifotis col. 13, ll. 57–65. Similarly, Mazel teaches:

If desired, a memory aid can be provided, for example in the form of numbers, letters, or other markings or with a calendar feature and/or calendar insert, designating the days in the treatment schedule in which the dosages can be administered. Alternatively, placebo dosages, or vitamin or dietary supplements, either in a form similar to or distinct from the pharmaceutical active dosages, can be included.

Mazel ¶ 77. The Geest Declaration compares the comprehension and adherence of two groups of patients, one of which uses a combination pack of risedronate and calcium supplement tablets, as claimed in Appellants' invention, and the other of which has separate packs of risedronate and calcium supplement tablets. Geest Decl. ¶ 13. However, as we have explained above, combination packs, such as those taught by Daifotis and Mazel, were already known in the art as memory aids at the time Appellants' application was filed. The Geest Declaration does not compare Appellants' claimed invention with the prior art and Appellants adduce no other evidence that their claimed invention demonstrates unexpected or surprising results when compared to these references. Thus, the results in the Geest Declaration are not due to the merits of the invention, but were already available in the prior art. We consequently affirm the Examiner's rejection of the claims.

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Application 13/325,170

DECISION

The Examiner's rejection of claims 24, 26, 29 and 34 as unpatentable under 35 U.S.C. § 103(a) is affirmed.

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). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED