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The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 12

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte PETER DICPINIGAITIS

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Appeal No. 1997-2829  
Application No. 08/456,090

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ON BRIEF

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Before WINTERS, WILLIAM F. SMITH and ROBINSON, Administrative Patent Judges.

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal from the final rejection of claims 1 through 13, all claims pending in the application.

I. Background

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A. Angiotensin converting enzyme (ACE) inhibitors are widely used in treating hypertension, congestive heart failure, acute myocardial infarction and diabetic nephropathy (Specification, page 1, lines 2-5).

B. One of the side effects often observed in patients taking ACE inhibitors is a persistent, dry cough that is refractory to most commonly prescribed cough suppressants (Specification, page 1, lines 5-7).

C. As acknowledged by appellant, baclofen is known in the prior art to have antitussive effects (Specification, page 1, lines 14-20).

## II. Representative Claims

Claims 1, 7 and 13 are illustrative of the subject matter on appeal and read as follows:

1. A method for the suppression of the cough which is associated with the administration of an ACE inhibitor which comprises administering an ACE cough suppressing amount of baclofen for a sufficient period of time to suppress the cough associated with the administration of the ACE inhibitor.

7. A pharmaceutical composition which comprises an ACE inhibiting effective amount of an ACE inhibitor and an amount of baclofen which is sufficient to inhibit the cough which is associated with the administration of an ACE inhibitor.

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13. A method for the suppression of the cough which is associated with the administration of an ACE inhibitor which comprises administering from 10 to 30 mg daily of baclofen for a period of time, which is about three days, in order to suppress the cough associated with the administration of the ACE inhibitor.

### III. References

The references relied on by the examiner are:

Kreutner et al. (Kreutner)                      5,006,560                      Apr. 9, 1991

A. J. Houston et al. (Houston), 112 British Journal of Pharmacology, Proceedings Supplement, 264 (May 1994)

### IV. Claim groupings

In the Appeal Brief (Paper No. 10, page 2), appellant sets forth these claim groupings:

Claims 1-6 stand or fall together.<sup>1</sup>

Claims 7-12 stand or fall together.

Claim 13 stands or falls separately.

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<sup>1</sup>Claim 6 does not positively recite the step of administering baclofen. Thus, claim 6 appears to be improper. In view of our disposition of this appeal, since claim 6 stands or falls with claim 1, we find it unnecessary to enter a new ground of rejection under 37 CFR § 1.196(b). However, if prosecution is resumed on this subject matter in a continuing application, the examiner should determine whether claim 6 meets the statutory requirements under 35 U.S.C. § 101 and 35 U.S.C. § 112, second paragraph.

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Appellant presents separate arguments with respect to each grouping, as required under 37 CFR § 1.192(c)(7) and (c)(8) (July 1996). See Brief, first full paragraph of page 5, with respect to claims 7-12; and paragraph bridging pages 4 and 5, with respect to claim 13.

#### V. Rejections

The claims stand rejected as follows:

Claims 1-6 and 13 under 35 U.S.C. § 103 as unpatentable over Kreutner in view of appellant's admission in the instant specification, page 1, first paragraph.

Claims 7-12 under 35 U.S.C. § 103 as unpatentable over Kreutner in view of appellant's admission in the instant specification, page 1, first paragraph, further in view of Houston.

We affirm the rejection of claims 1-6 and 13, and reverse the rejection of claims 7-12.

#### VI. Discussion

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A. Rejection of claims 7-12 under 35 U.S.C. § 103 as unpatentable over Kreutner in view of appellant's admission in the specification, page 1, first paragraph, and Houston.

1. The claimed subject matter is drawn to a pharmaceutical composition comprising an "ACE inhibiting effective amount" of an ACE inhibitor and a sufficient amount of baclofen to inhibit the cough associated with administering the ACE inhibitor.

2. To establish prima facie obviousness of the claimed subject matter, all claim limitations must be taught or suggested by the prior art. See In re Royka, 490 F.2d 981, 984, 180 USPQ 580, 583 (CCPA 1974). In this case, the prior art fails to disclose or suggest a composition comprising both an ACE inhibitor and baclofen.

3. The claimed composition comprises both an ACE inhibitor and baclofen. Specification, page 2, lines 9-23, and 30-37.

Kreutner discloses administering baclofen by intravenous or oral methods, such as a capsule or tablet, to suppress coughing (Kreutner, col. 4, lines 4-24). However, Kreutner neither discloses nor suggests a composition comprising both

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baclofen and an agent that induces coughing. Houston discloses injecting a rat with captopril (identified as an ACE inhibitor at page 2, line 25, of the instant specification); then injecting baclofen to inhibit water intake induced by systemic administration of the ACE inhibitor. Houston does not, however, disclose a composition comprising both baclofen and an ACE inhibitor. In the specification, page 1, first paragraph, appellant acknowledges that one of the side effects often observed in patients taking ACE inhibitors is a persistent, dry cough that is refractory to most commonly prescribed cough suppressants.

On this record, the examiner does not point to any reason, suggestion, or motivation stemming from the prior art which would have led a person having ordinary skill to a composition comprising both baclofen and an ACE inhibitor. Thus, the prior art fails to disclose or suggest the claimed composition.

The examiner's decision, rejecting claims 7-12 under 35 U.S.C. § 103, is reversed.

B. Rejection of claims 1-6 and 13 under 35 U.S.C. § 103 as unpatentable over Kreutner in view of appellant's admission in the specification, page 1, first paragraph.

1. The claimed subject matter is drawn to a method for suppression of coughing associated with the administration of an ACE inhibitor, which comprises administering an ACE cough suppressing amount of baclofen for a sufficient period of time to suppress the cough.

2. Kreutner teaches a method for treating cough in mammals by administering an antitussive effective amount of baclofen. Kreutner, col. 1, line 65, to col. 2, line 4. Kreutner teaches that baclofen, when used orally, parenterally or topically, can be administered in amounts ranging from about 0.1 mg/kg body weight to about 100 mg/kg body weight, preferably from about 0.3 mg/kg body weight to about 25 mg/kg body weight per day. A typical recommended dosage regimen is oral administration of from 5 mg/day to 5000 mg/day, preferably 10 mg/day to 1000 mg/day, in two or four divided doses to achieve relief of cough. Kreutner, col. 3, lines 48-57. Kreutner teaches that the determination of the proper dosage of baclofen for a particular situation is within the

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skill of the art (Kreutner, col. 3, lines 58-60). Kreutner teaches that the amount and frequency of the administration of baclofen will be regulated according to the judgment of the attending clinician with respect to the age, condition and size of the patient, and the severity of the symptom being treated (Kreutner, col. 3, line 66, to col. 4, line 3).

Kreutner does not specifically address coughs induced by the administration of an ACE inhibitor. However, Kreutner does not limit the source of the cough. According to Kreutner, baclofen has unexpectedly surprising activity as an antitussive agent (Kreutner, col. 1, lines 65-67). Baclofen has demonstrated cough suppressing activity significantly (about 14 to 40 times) better than codeine in the tests performed by Kreutner (Kreutner, col. 3, lines 2-5; col. 6, lines 8-12). Administering baclofen in an antitussive effective amount avoids the possible side effects caused by GABA-A agonism, such as motor-incoordination, confusion, light-headedness, and other adverse psychomotor and psychological effects (Kreutner, col. 1, lines 42-52; col. 1, line 67, to col. 2, line 2). Kreutner strongly suggests that

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baclofen can inhibit chemically, mechanically, or electrically-induced cough (Kreutner, col. 6, lines 45-51).

In the specification, page 1, first paragraph, appellant acknowledges that one of the side effects often observed in patients taking ACE inhibitors is a persistent, dry cough that is refractory to most commonly prescribed cough suppressants.

The examiner concludes that a person having ordinary skill in the art would have found it obvious to employ baclofen in treating coughs induced by ACE inhibitors because: (1) the antitussive activity of baclofen is broadly known in the art, as acknowledged by appellant in the specification, page 1, lines 14-20; (2) baclofen has unexpectedly surprising activity as an antitussive agent, Kreutner, col. 1, lines 65-67; (3) baclofen has demonstrated cough suppressing activity significantly (about 14 to 40 times) better than codeine in the tests performed by Kreutner, Kreutner, col. 3, lines 2-5; col. 6, lines 8-12; (4) administering baclofen in an antitussive effective amount avoids the possible side effects caused by GABA-A agonism, such as motor-incoordination, confusion, light-headedness, and other adverse psychomotor and

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psychological effects (Kreutner, col. 1, lines 42-52; col. 1, line 67, to col. 2, line 2); and (5) Kreutner strongly suggests that baclofen can inhibit chemically, mechanically, or electrically-induced cough (Kreutner, col. 6, lines 45-51). The examiner further states that "optimization of amounts of ingredients to be used is deemed within the skill of the artisan" (Answer, Paper No. 11, paragraph bridging pages 5 and 6).

3. With respect to Group I, claims 1-6, appellant argues the following:

a. Kreutner is silent respecting the treatment of coughs induced by ACE inhibitors ( Brief, page 2, line 28, to page 3, line 4).

However, as set forth in section VI-B2, supra, Kreutner does not limit the source of the cough. Kreutner strongly suggests that baclofen can inhibit chemically, mechanically, and electrically-induced cough (Kreutner, col. 6, lines 45-51). Further, as discussed, supra, Kreutner discloses that (1) baclofen has unexpectedly surprising activity as an antitussive agent (Kreutner, col. 1, lines 65-67); (2) baclofen has demonstrated cough suppressing activity

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significantly (about 14 to 40 times) better than codeine in the tests performed by Kreutner (Kreutner, col. 3, lines 2-5; col. 6, lines 8-12); and (3) administering baclofen in an antitussive effective amount avoids the possible side effects caused by GABA-A agonism (Kreutner, col. 1, lines 42-52; col. 1, line 67, to col. 2, line 2). As acknowledged by appellant in the specification, page 1, first paragraph, a persistent, dry cough is often observed as one of the side effects exhibited by patients taking ACE inhibitors. In our judgment, the method recited in appealed claim 1 would have been prima facie obvious to a person having ordinary skill in the art because that person would have had a reasonable expectation of successfully suppressing cough, induced by the administration of an ACE inhibitor, by administering baclofen. For obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

b. Appellant argues that (1) Kreutner does not teach administering baclofen on a continuous basis before antitussive activity is observed; and (2) Kreutner does not

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teach that it is necessary to continue the administration of baclofen beyond three days to provide relief from ACE inhibitor induced coughing (Brief, page 3, lines 11-21).

However, appealed claim 1 does not require the continuous administration of baclofen beyond three days. Claim 1 merely recites that baclofen be administered for "a sufficient period of time to suppress the cough associated with the administration of the ACE inhibitor." Appellant cannot rely on limitations that are not present in the claims. See In re Yamamoto, 740 F.2d 1569, 1571, 222 USPQ 934, 936 (Fed. Cir. 1984).

Further, even if claim 1 did require the continuous administration of baclofen beyond three days, that limitation would have been obvious to a person having ordinary skill in the art in view of the teachings of Kreutner. As set forth in section VI-B2, supra, Kreutner teaches that determination of the proper dosage of baclofen for a particular situation is within the skill of the art. The amount and frequency of the administration of baclofen will be regulated according to the judgment of the attending clinician with respect to the age, condition and size of the patient, and the severity of the

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symptom being treated (Kreutner, col. 3, line 58 through col. 4, line 3). Moreover, Kreutner discloses that reduction of cough frequency is dependent on the dose of baclofen. See Kreutner, Figs. 1A and 1B, and the accompanying text at col. 6, lines 4-21. Thus, the dosage of baclofen is a result-effective variable, and variation of dosage would be well within the skill of the ordinary worker in the art. In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). The persistent administration of an antitussive agent, such as baclofen, to treat a persistent cough would have been obvious to a person having ordinary skill in the art, in particular the attending clinician.

c. The Rule 132 Declaration of Peter Dicipinigaitis, filed 14 March 1996 (Paper No. 7), shows that the antitussive effect of baclofen on the cough induced by an ACE inhibitor is observed after three days. Declarant concludes that a single dose of baclofen has no effect on the cough induced by an ACE inhibitor. Based on the declaration, appellant argues that continuous administration of baclofen beyond three days

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constitutes an unobvious result (Brief, paragraph bridging pages 3-4). We disagree.

Appellant's reliance on the Rule 132 Declaration is misplaced for these reasons:

First, the declaration is insufficient because it is not commensurate in scope with claim 1. As set forth in section VI-B3-b, supra, appealed claim 1 does not require the continuous administration of baclofen beyond three days. Objective evidence of non-obviousness must be commensurate in scope with the claims. In re Kulling, 897 F.2d 1147, 1149, 14 USPQ2d 1056, 1058 (Fed. Cir. 1990).

Second, the evidence is insufficient because the continuous administration of baclofen beyond three days does not constitute an unexpected result. Appellant has not adequately taken into account the appropriate level of skill in this art. Contrary to appellant's comments at page 4, lines 2-3 of the Brief, Kreutner is not limited to administering a single dosage of baclofen. See section VI-B2, supra. In view of the teachings of Kreutner, a person having ordinary skill in the art, in particular the clinician, through routine experimentation, would have readily determined

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the dosage, e.g., the amount, frequency and duration of baclofen required to suppress coughing, such as that induced by ACE inhibitors. (If a headache persists after administering a single dosage of aspirin, more aspirin is usually taken until the headache is gone.)

The rejection of claims 1-6 under 35 U.S.C. § 103 over Kreutner is affirmed.

4. Appellant argues that claim 13 is patentable for the following reasons:

a. Claim 13 recites administering from 10 to 30 mg daily of baclofen for about three days to suppress the cough associated with the administration of an ACE inhibitor; and

b. The Rule 132 Declaration provides evidence that baclofen has no effect on ACE inhibitor induced coughing until three days have elapsed. See Brief, Paper No. 10, paragraph bridging pages 4 and 5.

However, as set forth in section VI-B2, supra, Kreutner discloses that baclofen can be administered from 5 to 5000 mg/day, preferably from 10 to 1000 mg/day, to achieve relief of cough (Kreutner, col. 3, lines 53-57). Appellant at page 3, lines 21-23 of the Brief, acknowledges that this "embraces"

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the range recited in appealed claim 13. For the reasons set forth in section VI-B3-b, supra, the dosage limitation of baclofen recited in appealed claim 13 would have been well within the level of skill in this art and obvious over Kreutner. For the reasons set forth in section VI-B3-c, supra, the Rule 132 Declaration is insufficient to show that the dosage limitation recited in claim 13 constitutes an unexpected result.

The rejection of claim 13 under 35 U.S.C. § 103 is affirmed.

#### VII. Conclusion

In conclusion, for the reasons set forth in the body of this opinion, we affirm the examiner's decision rejecting

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claims 1 through 6 and 13, and reverse the examiner's decision  
rejecting claims 7 through 12.

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

AFFIRMED-IN-PART

SHERMAN D. WINTERS	)	
Administrative Patent Judge	)	
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WILLIAM F. SMITH	)	BOARD OF PATENT
Administrative Patent Judge	)	APPEALS AND
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DOUGLAS W. ROBINSON	)	
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