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EX A

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF MICHIGAN
SOUTHERN DIVISION

CARACO PHARMACEUTICAL LABORATORIES, LTD.,

Plaintiff,

v.

FOREST LABORATORIES, INC., FOREST LABORATORIES HOLDINGS, LTD. and H. LUNDBECK A/S,

Defendants.
_____/

Case: 4:07-cv-10737
Assigned To: Gadola, Paul V
Referral Judge: Scheer, Donald A
Filed: 02-20-2007 At 03:21 PM
CMP CARACO PHARMACEEUTICAL VS FORES T LAB ET AL (LE)

COMPLAINT

Plaintiff Caraco Pharmaceutical Laboratories, Ltd. ("Caraco"), by its attorneys, for its Complaint against Forest Laboratories, Inc., Forest Laboratories Holdings, Ltd., and H. Lundbeck A/S (collectively, "Defendants") alleges as follows:

INTRODUCTION

1. Caraco brings, and is entitled by statute to maintain, this action for declaratory judgment of patent non-infringement under, inter alia, the federal Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, and 21 U.S.C. § 355(j)(5)(C)(i), which is part of the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act ("FFDCA"), as amended by Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003) ("MMA").

2. This action arises out of, *inter alia*, Caraco's submission of an Abbreviated New Drug Application ("ANDA") to the U.S. Food and Drug Administration ("FDA") seeking approval to market a generic version of Defendants' brand-name anti-depression medication LEXAPRO®, known generically as escitalopram oxalate.

3. Defendants purport to own U.S. Patent Nos. Re. 34,712 ("the '712 patent") and 6,916,941 ("the '941 patent"). Upon submission by Defendants, the '712 and '941 patents were listed in FDA's compilation of approved drigs and their respective patents entitled "Approved Drug Products With Therapuetic Equivalence Evaluations", commonly referred to as the "Orange Book". As a consequence of such Orange Book listing, Defendants maintain, and have affirmatively represented to the world, that the '712 and '941 patents claim the approved drug LEXAPRO®, or a method of using that drug, and that a claim for patent infringement could reasonably be asserted against any generic ANDA applicant, including Caraco, attempting to market a generic escitalopram product before expiration of the '712 and '941 patents.

4. Caraco seeks to market a generic escitalopram product before the expiration of the '712 and '941 patents. Therefore, as required by the FFDCA, Caraco has certified to FDA that its ANDA products will not infringe any valid or enforceable claims of the '712 and '941 patents and has further notified Defendants of the legal and factual bases for those certifications. Caraco's submission of the so-called paragraph IV certifications to the '712 and '941 patents constitutes an artificial act of patent infringement putting Caraco at considerable risk of being sued by Defendants both before and after market entry.

5. This regulatory submission creates the necessary case or controversy and subject matter jurisdiction for Defendants to sue Caraco – and for Caraco to obtain declaratory judgment against Defendants – regarding infringement of the '712 and '941 patents.

6. In a separate lawsuit, *Forest Laboratories, Inc., Forest Laboratories Holdings, Ltd., and H. Lundbeck A/S. v. Caraco Pharmaceutical Laboratories, Ltd.*, Case No. 2:06-cv-13143 (BAF) (MKM), Defendants, in fact, sued Caraco for infringement of the '712 patent. Defendants, to date, have not sued Caraco for infringement of the '941 patent.

7. Caraco has satisfied all substantive requirements for approval of its ANDA, and is prepared to begin commercial marketing of its competing generic product prior to expiration of the '712 and '941 patents. But Caraco's approval has been delayed and Caraco is presently prevented from competing in the escitalopram market by purported generic marketing exclusivities arising out of the '712 and '941 patents. In *Forest Laboratories, Inc., et al. v. Caraco Pharmaceutical Laboratories, Ltd.*, Case No. 2:06-cv-13143, Caraco is currently litigating and will obtain a court judgment as to the validity, enforceability and/or infringement of the '712 patent. A declaratory judgment from this Court as to the '941 patent can alleviate Caraco's harm and allow Caraco to obtain approval of its product and compete in the lucrative escitalopram market.

8. In addition to a court order finding the '712 patent invalid and/or not infringed, unless Caraco obtains a similar court order on the '941 patent, Caraco faces potentially enormous infringement liability if it markets its generic product prior to expiration of the '941 patent. Only a declaratory judgment from this Court can alleviate this harm and allow Caraco to obtain approval of its product and compete in the escitalopram market free from such potential liability.

9. Accordingly, there is an actual, substantial, and continuing justiciable case and controversy between Caraco and Defendants regarding the '941 patent, over which this Court can and should exercise jurisdiction and declare the rights of the parties. Caraco is entitled by law to bring and maintain this action for declaratory judgment of patent non-infringement under the Declaratory Judgment Act and the MMA where, as here, Defendants did not sue Caraco within 45 days of receipt of Caraco's notice of paragraph IV certification to the '941 patent, and Caraco has offered Defendants an Offer of Confidential Access to Caraco's ANDA for generic escitalopram product.

10. Caraco is entitled to a judicial declaration that the manufacture, sale, offer for sale, use, or importation of Caraco's proposed generic escitalopram product does not and will not infringe the '941 patent. Absent the exercise of jurisdiction by this Court and such declaratory relief, Caraco and the American public will be irreparably harmed by the substantial delay in the market entry and availability of lower-priced generic escitalopram.

THE PARTIES

11. Plaintiff Caraco Pharmaceutical Laboratories, Ltd. is a Michigan corporation having a principal place of business at 1150 Elijah McCoy Drive, Detroit, Michigan 48202.

12. Defendant Forest Laboratories, Inc. is a Delaware corporation having a principal place of business at 909 Third Avenue, New York, New York 10022.

13. Defendant Forest Laboratories Holdings, Ltd. is an Irish corporation having offices at Milner House, 18 Parliament Street, Hamilton JM11, Bermuda.

14. Defendant H. Lundbeck A/S is a Danish corporation having a principal place of business at Ottiliavej 9, DK-2500 Valby, Copenhagen, Denmark.

U.S. PATENT NO. 6,916,941

15. Upon information and belief, on July 12, 2005, the '941 patent, titled "Crystalline composition containing escitalopram" – a copy of which is attached hereto as Exhibit A – was issued to H. Lundbeck A/S as assignee.

16. Upon information and belief, the '941 patent is scheduled to expire on January 25, 2023.

17. Upon information and belief, H. Lundbeck A/S is the owner of the '941 patent.

18. Upon information and belief, Forest Laboratories Holdings, Ltd. is the exclusive licensee of the '941 patent and Forest Laboratories, Inc. holds New Drug Application ("NDA") No. 21323 on LEXAPRO® brand escitalopram oxalate tablet products.

19. Upon information and belief, Forest Laboratories Holdings, Ltd. has appointed Forest Laboratories, Inc. its exclusive distributor of LEXAPRO® brand escitalopram oxalate products in the United States.

20. Upon information and belief, Defendants have the right to sue for any infringement of the '941 patent.

JURISDICTION AND VENUE

21. Substantial, present, genuine and justiciable controversies exist between Defendants and Caraco regarding the '941 patent.

22. This action arises under, *inter alia*, the Patent Laws of the United States, 35 U.S.C. §§ 1 *et seq.*; the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202; and the MMA (21 U.S.C. § 355(j)(5)(C)(i) and 35 U.S.C. § 271(e)(5)).

23. This Court has original jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331 and 1338(a), because it involves substantial claims arising under the United States Patent Act, 35 U.S.C. §§ 1 *et seq.*; under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, because it is an actual controversy concerning the '941 patent; and under the MMA (21 U.S.C. § 355(j)(5)(C)(i) and 35 U.S.C. § 271(e)(5)), because Congress has directed that district courts maintain and exercise jurisdiction in such cases.

24. This Court can and should declare the rights and legal relations of the parties regarding the '941 patent pursuant to, *inter alia*, the Declaratory Judgment Act, 28 U.S.C. §§ 2201, 2202, and the MMA (21 U.S.C. § 355(j)(5)(C)(i) and 35 U.S.C. § 271(e)(5)).

25. Caraco has the statutory right to bring and maintain this declaratory judgment action under 21 U.S.C. § 355(j)(5)(C)(i). This Court can and should exercise its declaratory judgment jurisdiction over Caraco's claims pursuant to 35 U.S.C. § 271(e)(5).

26. Upon information and belief, this Court has personal jurisdiction over Defendants because Defendants conduct substantial business in, and have regular and systematic contact with, this District.

27. Upon information and belief, Defendants maintain such a continuous and systematic contact with the State of Michigan and this District by conducting substantial, regular and systematic business therein through the marketing and sales of their pharmaceutical products, including LEXAPRO® – the purported commercial embodiment of the '941 patent – to allow this Court to reasonably exercise personal jurisdiction over Defendants.

28. This Court also has personal jurisdiction over Defendants because Defendants have submitted to the jurisdiction of this Court in a prior related litigation, *Forest Laboratories, Inc., Forest Laboratories Holdings, Ltd., and H. Lundbeck A/S. v. Caraco Pharmaceutical Laboratories, Ltd.*, Case No. 2:06-cv-13143 (BAF) (MKM), which is currently pending in this Court.

29. Upon information and belief, Defendants purposefully avail themselves of the privilege of doing business in the State of Michigan and in this District.

30. Venue is proper in this District under 28 U.S.C. § 1400(b). Venue is also proper in this District under 28 U.S.C. § 1391 because, *inter alia*, Defendants are subject to personal jurisdiction in this District and because Defendants are alien corporations.

BACKGROUND

I. Regulatory Framework

A. FDA Approval Of New Drug Applications (NDAs).

31. The Federal Food, Drug, and Cosmetic Act ("FFDCA"), 21 U.S.C. § 301 *et seq.*, as amended by the Hatch-Waxman Amendments and Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA"), sets forth the rules that the Food and Drug Administration ("FDA") follows when considering whether to approve the marketing of both brand-name and generic drugs.

32. Under the FFDCA, an applicant seeking to market a new brand-name drug must prepare an NDA for consideration by FDA. *See* 21 U.S.C. § 355.

33. The NDA must include, among other things, the number of any patent that claims the "drug" or a "method of using [the] drug" for which the NDA was submitted and for which a claim of patent infringement could reasonably be asserted against an unauthorized party. *See* 21 U.S.C. § 355(b)(1), -(c)(2); 21 C.F.R. § 314.53(b), -(c)(2).

34. Upon approval of the NDA, FDA publishes patent information for the approved drug in the "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the "Orange Book." *See* 21 U.S.C. § 355(j)(7)(A)(iii).

35. By filing an NDA and submitting a patent for listing in the Orange Book, the NDA-holder/patent owner, by law, necessarily maintains that the listed patent claims the approved NDA drug, or a method of using that drug, and that an infringement suit could reasonably be asserted against anyone who engages in the manufacture, use, or sale of the drug, and, in particular, against any company that is seeking to make a generic bioequivalent of the NDA drug before patent expiration.

36. Thus, the NDA-holder/patent owner necessarily puts all prospective generic ANDA applicants on notice that a suit for infringement can and will be asserted against any ANDA applicant that attempts to seek approval for and market a generic version of the NDA drug before patent expiration.

37. Such conduct by the NDA-holder/patent owner gives rise to a real and concrete belief on the generic applicant's part that it will face an infringement suit, or the threat of one, if it attempts to seek approval for or to market a generic version of the NDA drug before patent expiration.

B. Generic Competition – Abbreviated New Drug Applications (ANDA).

38. Generic drugs are versions of brand-name prescription drugs that typically contain the same active ingredients, but not necessarily the same inactive ingredients, as the brand-name original.

39. In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Amendments to the FFDCA. *See* Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. § 355 and 35 U.S.C. §§ 156, 271(e)).

40. Congress passed the Hatch-Waxman Amendments, which simplified the procedure for obtaining approval of generic drugs, for the purpose of decreasing the cost of pharmaceuticals through increased competition and to expedite the marketing of lower-priced generic drug products. Under the Hatch-Waxman Amendments, a generic manufacturer submits what is called an Abbreviated New Drug Application ("ANDA").

41. To receive approval of its ANDA, an applicant must show, *inter alia*, that its generic drug is "bioequivalent" to the listed reference drug. *See* 21 U.S.C. § 355(j)(4)(F).

42. An ANDA also must contain a "certification" to each patent that the NDA holder has submitted to FDA for listing in the Orange Book in connection with the listed reference drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.94(a)(12).

43. A so-called "paragraph IV" certification asserts that the listed patent is invalid, unenforceable, and/or will not be infringed and, on that basis, seeks FDA approval of the generic product prior to patent expiration. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV); 21 C.F.R. § 314.94(a)(12).

44. The submission of a paragraph IV certification has two important consequences.

45. First, a generic applicant that is first to submit an ANDA containing a paragraph IV certification for a listed patent is entitled to 180 days of generic market exclusivity during which no other competing generic drug products may be marketed. 21 U.S.C. § 355(j)(5)(B)(iv). This statutory benefit to the first filer is commonly known as "180-day exclusivity."

46. In particular, the statutory provision of the FFDCA applicable here provides that "[i]f the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this section [containing] such a certification, the application shall be made effective not earlier than one hundred and eighty days after" the earlier of: (a) the first commercial marketing of that ANDA applicant's proposed drug; or, (b) a court decision – whether it involves the first applicant or not – that the particular patent that is the subject of the paragraph IV certification is invalid or not infringed. 21 U.S.C. § 355(j)(5)(B)(iv). Thus, unless a subsequent generic applicant can obtain a court decision of noninfringement and/or invalidity as Congress intended, the approval of its ANDA can be delayed indefinitely by the purported exclusivity of the first-filer.

47. Second, the submission of a paragraph IV certification for a listed patent constitutes an artificial act of infringement that creates the necessary case or controversy and subject matter jurisdiction to enable an NDA-holder/patent owner to file, and a district court to resolve, an action for patent infringement – before the generic drug is actually made, used, or sold – to determine whether the generic drug, if marketed and sold in accordance with the ANDA, would infringe the relevant patent.

48. The submission of a paragraph IV certification likewise creates the necessary case or controversy and subject matter jurisdiction for an ANDA applicant to file a declaratory judgment action against the NDA-holder/patent owner if the ANDA applicant is not sued on the listed patent within the applicable 45-day period.

49. An applicant submitting an ANDA containing a paragraph IV certification must notify both the NDA holder and patent owner of its paragraph IV certification. *See* 21 U.S.C. § 355(j)(2)(B)(i).

50. Upon receiving notice of the paragraph IV certification, the NDA holder/patent owner has 45 days in which to file an infringement suit against the generic manufacturer. *See* 21 U.S.C. § 355(j)(5)(B)(iii); 35 U.S.C. § 271(e)(2)(A).

51. The NDA holder/patent owner's filing of a lawsuit prior to the expiration of 45 days prevents FDA from issuing final approval of the generic maker's ANDA for a period of 30 months, absent certain exceptions. *See* 21 U.S.C. § 355(j)(5)(B)(iii).

C. ANDA-Filer May Bring A Declaratory Judgment Action

52. On December 8, 2003, the MMA was signed into law. Title XI of the MMA, labeled "Access to Affordable Pharmaceuticals," amended provisions of the FFDCA and, in particular, the Hatch-Waxman Amendments.

53. Under the MMA, an ANDA applicant who has filed a paragraph IV certification is statutorily entitled to institute and maintain an action for declaratory judgment against an NDA-holder/patent owner if: (1) the 45-day period has passed since notice of the paragraph IV certification was received; (2) neither the patent owner nor the NDA-holder/patent owner brought an action for infringement of the patent within the 45-day period; and, (3) the notice of paragraph IV certification contains an Offer of Confidential Access to the ANDA. 21 U.S.C. §§ 3550(j)(5)(C)(i)(I)(aa)-(cc).

54. Once these three conditions are met, the MMA specifically and unequivocally provides that an ANDA applicant "may, in accordance with section 2201 of Title 28 [of the United States Code] bring a civil action under such section against the owner or holder referred to in such subclause ... for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval ...." 21 U.S.C. § 355(j)(5)(C)(i)(II).

55. An ANDA applicant may exercise its right to file and maintain a declaratory judgment action under the MMA regardless of whether or not the Offer of Confidential Access to Application is accepted.

56. The new declaratory judgment provision contained in the MMA, Section 1101 of the MMA, 117 Stat. 2066, 2454-2456, applies to all ANDAs pending on or after December 8, 2003, which includes this proceeding.

57. Congress's intent in amending 21 U.S.C. § 355 and 35 U.S.C. § 271(e) was to extend to ANDA applicants, like Caraco here, the right to file and maintain a declaratory judgment action for patent noninfringement and/or invalidity against an NDA holder/patent owner, and to direct the district court to exercise subject matter jurisdiction in such an action.

58. The purpose of this provision was two-fold. First, Congress enacted the declaratory judgment provision to allow generic applicants to obtain court decisions that would expedite the introduction of generic drugs by allowing the generic applicant to obtain approval of its ANDA and clear up any bottleneck in the market created by another applicant's 180-day exclusivity.

59. The FFDCA provides that the first applicant to file a substantially complete ANDA containing a paragraph IV certification to a listed patent will be eligible for a 180-day period of exclusivity beginning either from the date it begins commercial marketing of the generic drug product, or from the date of a court decision finding the listed patent invalid, unenforceable or not infringed, whichever is first.

60. These events – first commercial marketing and a court decision – are often called triggering events, because under the statute they can trigger the beginning of the 180-day exclusivity period.

61. The 180-day exclusivity can begin to run, with a court decision by any applicant, even before the first applicant has received approval for its ANDA or before the first applicant has begun commercial marketing of the ANDA product. In that case, some, or all, of the 180-day exclusivity period could expire without the first ANDA applicant marketing its generic drug.

62. Conversely, if there is no court decision on a listed patent and the first applicant does not begin commercial marketing of the generic drug, there may be prolonged or indefinite delays in the beginning of the first applicant's 180-day exclusivity period.

63. Until an eligible ANDA applicant's 180-day exclusivity period has been triggered (and expires), FDA cannot approve subsequently submitted ANDAs for the same drug, even if the later ANDAs are otherwise ready for approval and the applicants are willing to immediately begin marketing.

64. By specifically allowing declaratory actions under these circumstances, Congress intended that full generic competition would not be delayed indefinitely by the first filer's 180-day exclusivity period. A declaratory action by a subsequent ANDA filer can result in a court decision that would trigger the first filer's 180-day exclusivity period, thereby clearing the way for approval of the subsequent ANDA filer.

65. Second, Congress intended to allow generic applicants to obtain patent certainty before marketing their generic products in order to avoid potentially catastrophic infringement damages.

66. Accordingly, if the NDA holder/patent owner does not file such a suit, the ANDA applicant can file and maintain a suit for declaratory judgment against the NDA-holder/patent owner to obtain patent certainty. Indeed, Congress explicitly mandated that an ANDA-filer is entitled to maintain a declaratory judgment action when it is not sued. 21 U.S.C. § 355(j)(5)(C).

67. Similarly, if the NDA holder/patent owner files a lawsuit, but fails to assert a patent that was the subject to an Orange Book listing and paragraph IV certification, the ANDA-filer is entitled to file and maintain a declaratory action against the NDA holder/patent owner to obtain patent certainty on the non-asserted patent.

II. Caraco's ANDA No. 78-219

A. Caraco Has The Right To Bring Declaratory Lawsuit On The '941 Patent

68. In March 2006, Caraco filed an ANDA (No. 78-219) with FDA seeking generic approval for 5, 10, and 20 mg tablets of escitalopram oxalate (the "ANDA Products").

69. Defendants listed the '712 patent and the '941 patent in the Orange Book in connection with NDA No. 21323 and the brand name drug LEXAPRO®, which comprises the active ingredient escitalopram oxalate.

70. By listing the '712 and '941 patents in the Orange Book, Defendants maintain, and have affirmatively represented to the world, that the '712 and '941 patents claim LEXAPRO®, or a method of using that drug, and that an infringement suit could reasonably be asserted against any generic ANDA applicant, including Caraco, that attempts to seek approval for, and market, a generic version of LEXAPRO® before the expiration of the '712 and '941 patents. The listing of the '712 and '941 patents in the Orange Book alone objectively creates the necessary case or controversy and subject matter jurisdiction for an ANDA-filer who makes a paragraph IV certification as to the '712 and '941 patents.

71. Because Caraco seeks FDA approval to market its ANDA Products before expiration of the '712 and '941 patents, Caraco's ANDA includes paragraph IV certifications to both the '712 and '941 patents.

72. On May 24, 2006, Caraco sent to Defendants a statutorily-required notice letter of its paragraph IV certifications, which contains a detailed factual and legal statement as to why the '712 and '941 patents are invalid, unenforceable, and/or not infringed by Caraco's ANDA Products.

73. Upon information and belief, Defendants received Caraco's notice letter of its paragraph IV certifications on May 24, 2006.

74. On July 10, 2006, Defendants filed a patent infringement lawsuit against Caraco, alleging that Caraco's ANDA Products would infringe the '712 patent. That lawsuit is currently pending in this Court.

75. Although a case or controversy exists between the parties on the '941 patent, Defendants did not bring a lawsuit that Caraco's ANDA Products would infringe the '941 patent.

76. Caraco, on its notice letter and as required under 21 U.S.C. § 355(i)(5)(C), extended to Defendants an Offer of Confidential Access to Application to access certain information in Caraco's ANDA for escitalopram product.

77. By providing this Offer of Confidential Access to Application, and because Defendants did not sue Caraco on the '941 patent within 45 days of receipt of Caraco's notice of paragraph IV certification, Caraco is statutorily entitled to file and maintain a declaratory judgment action against Defendants under 28 U.S.C. §§ 2201 and 2202, pursuant to 21 U.S.C. § 355(j)(5)(C).

B. Caraco's Need To Obtain Court Judgment On The '941 Patent

78. Caraco is not only entitled to bring this lawsuit but requires the decision of this lawsuit to avoid indefinite delays in its approval of ANDA No. 78-219.

79. Upon information and belief, Caraco is not the first ANDA filer on either the '712 patent or the '941 patent.

80. Upon information and belief, Ivax Corporation is the first ANDA filer with respect to each of the '712 and '941 patents, and, thus, arguably is entitled to a separate 180-day period of exclusivity on each of the '712 and '941 patents.

81. If this is proven true, generic competition for escitalopram products may be delayed until 180 days after expiration of the '941 patent in 2023, unless Ivax begins commercial marketing of its generic escitalopram product prior to the '941 patent's expiration date. Defendants refusal to litigate the validity and/or noninfringement of the '941 patent is purposefully preventing a court decision of invalidity, unenforceability and/or noninfringement on the '941 patent, which would trigger Ivax's 180-day exclusivity period for the '941 patent, thereby allowing generic competition to the benefit of both Caraco and the American public.

82. Moreover, until and unless Caraco obtains a court decision of noninfringement and/or invalidity on the '941 patent, it faces potentially enormous infringement liability if it commences marketing before the '941 patent expires. Caraco can alleviate this harm and obtain patent certainty only through a declaratory judgment from this Court on the '941 patent.

COUNT I
Declaration of Noninfringement of the '941 Patent

83. Caraco realleges and incorporates by reference the allegations of Paragraphs 1-82.

84. This Declaratory Action arises under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq.* and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, pursuant to 21 U.S.C. § 355(j)(5)(C), and seeks a declaration that one or more claims of the '941 patent will not be infringed by the manufacture, use, or sale of Caraco's ANDA Products.

85. A present, genuine, and justiciable controversy exists between Defendants and Caraco regarding, *inter alia*, the issue of whether the manufacture, use, or sale of Caraco's ANDA Products would infringe one or more claims of the '941 patent.

86. The manufacture, use, or sale of Caraco's ANDA Products would not infringe the claims of the '941 patent.

87. Caraco is entitled to a declaration that the manufacture, use, or sale of its ANDA Products would not infringe the claims of the '941 patent.

Prayer for Relief

WHEREFORE, Defendant Caraco Pharmaceutical Laboratories, Ltd. respectfully requests that this Court enter a Judgment and Order in its favor and against Defendants as follows:

(a) declaring that Caraco has not infringed and that Caraco's manufacture, use, or sale of products covered by ANDA No. 78-219 would not infringe the claims of U.S. Patent No. 6,916,941;

(b) declaring that this is an exceptional case under 35 U.S.C. § 285 and awarding Caraco its attorneys' fees, costs, and expenses in this action; and

(c) awarding Caraco any further and additional relief as the Court deems just and proper.

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US006916941B2

(12) **United States Patent**
Christensen et al.

(10) **Patent No.: US 6,916,941 B2**
(45) **Date of Patent: Jul. 12, 2005**

(54) **CRYSTALLINE COMPOSITION CONTAINING ESCITALOPRAM**

(75) Inventors: **Troels Volsgaard Christensen**, Holbæk (DK); **Ken Liljegren**, Værløse (DK); **Michiel Onne Elema**, København Ø (DK); **Lene Andresen**, Rødovre (DK); **Shashank Mahashabde**, Kendall Park, NJ (US); **Sebastian P. Assenza**, Fort Salonga, NY (US)

(73) Assignee: **H. Lundbeck A/S**, Valby-Copenhagen (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 18 days.

(21) Appl. No.: **10/403,453**

(22) Filed: **Mar. 31, 2003**

(65) **Prior Publication Data**

US 2003/0212128 A1 Nov. 13, 2003

Related U.S. Application Data

(63) Continuation of application No. PCT/DK02/00513, filed on Jul. 25, 2002.

(30) **Foreign Application Priority Data**

Jul. 31, 2001 (DK) ..... PA 2001 01164

(51) **Int. Cl.**[7] **C07D 307/78**; C07D 307/87; A61K 31/343

(52) **U.S. Cl.** **549/467**; 549/469; 514/469

(58) **Field of Search** 549/467, 469; 514/469

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(74) *Attorney, Agent, or Firm*—Darby & Darby

(57) **ABSTRACT**

Crystalline particles of escitalopram oxalate with a particle size of at least 40 μm is disclosed. Method for the manufacture of said crystalline particles and pharmaceutical compositions comprising said crystalline particles are also disclosed.

47 Claims, No Drawings

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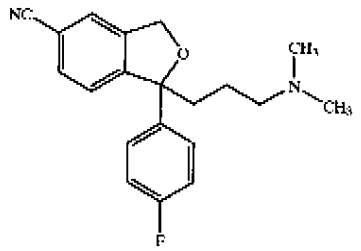
CRYSTALLINE COMPOSITION CONTAINING ESCITALOPRAM

This application is a continuation of International Application No. PCT/DK02/00513 filed Jul. 25, 2002. The prior application is hereby incorporated by reference in its entirety.

The present invention relates to crystalline preparations of the oxalate salt of the compound escitalopram (INN-name), which is the S-enantiomer of the well-known antidepressant drug citalopram, i.e. (S)-1-[3-(dimethylamino) propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile oxalate.

BACKGROUND OF THE INVENTION

Citalopram is a well-known antidepressant drug that has the following structure:



It is a selective, centrally active serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitor, accordingly having antidepressant activities.

Citalopram was first disclosed in DE 2,657,013, corresponding to U.S. Pat. No. 4,136,193. This patent publication describes the preparation of citalopram by one method and outlines a further method, which may be used for preparing citalopram. The citalopram prepared was isolated in crystalline form as the oxalate, the hydrobromide and the hydrochloride salt, respectively. Furthermore, the citalopram base was obtained as an oil (B.P. 175° C./0.03 mmHg). The publication also outlines the manufacture of tablets containing salts of citalopram. Citalopram is marketed as the hydrobromide and the hydrochloride, respectively.

Escitalopram, the pharmaceutical activity thereof and crystalline escitalopram oxalate are disclosed in U.S. Pat. No. 4,943,590. Methods for preparation of pharmaceutical preparations of escitalopram are outlined.

Citalopram is marketed in a number of countries as a tablet prepared by compression of granulated citalopram hydrobromide, lactose and other excipients. It is well recognised that preparation of tablets with a reproducible composition requires that all the dry ingredients have good flow properties. In cases, where the active ingredient has good flow properties, tablets can be prepared by direct compression of the ingredients. However, in many cases the particle size of the active substance is small, the active substance is cohesive or has poor flow properties.

Further, active substances with a small particle size mixed with excipients having a larger particle size will typically segregate or de-mix during the tabletting process. The problem of small particle size and poor flowability is conventionally solved by enlarging the particle size of the active substance, usually by granulation of the active ingredient either alone or in combination with a filler and/or other conventional tablet ingredients.

One such granulation method is the "wet" granulation process. Using this method, the dry solids (active ingredients, filler, binder etc.) are blended and moistened with water or another wetting agent (e.g. an alcohol) and agglomerates or granules are built up of the moistened solids. Wet massing is continued until a desired homogenous particle size has been achieved whereupon the granulated product is dried.

An alternative to the "wet" granulation method is the "melt" granulation, which is also known as the "thermal plastic" granulation process, where a low melting solid is used as the granulation agent. Initially, the dry solids are blended and heated until the binder melts. As the binder is liquefied and spreads over the surface of the particles, the particles will adhere to each other and form granules. The binder solidifies upon cooling forming a dry granular product.

Wet granulation as well as melt granulation are energy intensive unit operations requiring complicated and expensive equipment as well as technical skill.

If the active ingredient, however, has suitable flow properties, then the granulation step can be avoided and tablets may be prepared by direct compression which is a cheaper production method.

The process used for the preparation of citalopram hydrobromide results in a product with a very small particle size around 2–20 μm that, as many other particulate products with a small particle size, has very poor flow properties. Thus, in order to achieve appropriate dosing of the citalopram hydrobromide during tabletting, it was considered necessary to make a granulate of citalopram hydrobromide with larger particle size and improved flow properties.

The citalopram tablet that is marketed is a tablet made from granulated citalopram hydrobromide with various excipients.

We have found that escitalopram has significantly different solubility and salt formation properties from the citalopram racemate. For example, the only pharmaceutically crystalline salt known so far is the oxalate, whereas the citalopram racemate forms crystalline hydrobromide and hydrochloride salts as well.

The escitalopram oxalate product prepared by crystallisation from acetone as outlined in U.S. Pat. No. 4,943,590 has, as the citalopram hydrobromide product described above, a very small particle size around 2–20 μm resulting in similarly poor flow properties.

In view of the fact that direct compression is much simpler and cheaper than the processes involving granulation there is a desire for larger crystals of escitalopram or pharmaceutical acceptable addition salts thereof.

Extensive laboratory and full-scale research has resulted in a new and inventive crystallisation process producing larger crystalline particles of escitalopram oxalate, i.e. particles of a size comparable to the size of the filler. Said particles are useful for the manufacture of directly compressed tablets. Accurate dosing in capsules may also be with such large particles.

OBJECTS OF THE INVENTION

It is the object of the present invention to provide large crystalline particles of escitalopram oxalate suitable for use in direct compression.

A second object of the invention is to provide a method for manufacture of large crystalline particles of escitalopram oxalate.

A third object of the invention is to provide a novel pharmaceutical unit dosage form containing large crystalline particles of escitalopram oxalate, wherein said unit dosage form may be a tablet, which preferably may be prepared by direct compression, or a capsule.

SUMMARY OF THE INVENTION

The invention then, inter alia, comprises the following, alone or in combination:

Crystalline particles of escitalopram oxalate with a median particle size of at least 40 μm and suitable for use in a solid unit dosage form.

A method for the manufacture of crystalline particles of escitalopram oxalate having a median particle size of at least 40 μm and suitable for use in a solid unit dosage form wherein said method comprises that a solution of escitalopram oxalate in a suitable solvent system at a first temperature is gradually cooled down to a second temperature maintaining a controlled cooling profile and seeding the crystallisation batch by addition of crystals of escitalopram oxalate at least once during the cooling and followed by a holding time at said second temperature whereupon said crystals are isolated by conventional solid/liquid separation techniques.

A solid unit dosage form comprising escitalopram prepared by direct compression of a mixture of escitalopram base or a pharmaceutically acceptable salt thereof and pharmaceutically acceptable excipients, or by filling of said mixture in a hard gelatine capsule.

The direct compression of escitalopram, a filler and other pharmaceutically acceptable excipients into tablets has the great advantage, that the granulation and a drying step is avoided. Further, as the granulation step is avoided, it is no longer necessary to add a binding agent.

As used herein, "escitalopram oxalate" means any addition salt consisting of escitalopram, oxalic acid and optionally water. Examples of such salts are the hydrogen oxalate salt of escitalopram, i.e. the salt consisting of one molecule of escitalopram per molecule of oxalic acid, as well as the oxalate salt of escitalopram, i.e. the salt consisting of two molecules of escitalopram per molecule of oxalic acid.

As used herein, "crystalline particles" means any combination of single crystals, aggregates and agglomerates.

As used herein, "direct compression" means that the solid unit dosage form is prepared by compression of a simple mixture of the active ingredient and excipients, without the active ingredient having been subjected to an intermediate granulation process in order to embed it in a larger particle and improve its fluidity properties.

As used herein, "binder" means an agent, which is used in wet or melt granulation processes and acts as a binder in the granulated product.

As used herein, "particle size distribution" means the cumulative volume size distribution of equivalent spherical diameters as determined by laser diffraction at 1 bar dispersive pressure in a Sympatec Helos equipment. "Median particle size", correspondingly, means the median of said particle size distribution.

As used herein, "refluxing temperature" means the temperature at which the solvent or solvent system refluxes or boils at atmospheric pressure.

As used herein, "cooling profile" means the temperature of the crystallisation batch as a function of time.

As used herein, "cooling rate" means the decrease in temperature per time unit.

Thus in one embodiment of the present invention the crystalline particles of escitalopram oxalate have a median particle size of at least 40 μm, preferably in the range of 50–200 μm.

Flow, segregation and demixing properties and, hence, the suitability of the escitalopram oxalate crystals for direct compression depend, besides the median particle size, on the particle side distribution.

In another embodiment of the present invention crystalline particles of escitalopram oxalate having a median particle size of at least 40 μm, preferably in the range of 50–200 μm, and suitable for use in a solid unit dosage form are crystallised from a solution of escitalopram oxalate in a suitable solvent system. Said solvent system may comprise one or more alcohols and optionally water, preferably the solvent system is ethanol. Escitalopram oxalate is preferably dissolved in the solvent system at a temperature in the range between 50° C. and the refluxing temperature of the solvent system, preferably between 60° C. and the refluxing temperature and more preferred between 70° C. and the refluxing temperature, suitably the escitalopram oxalate is dissolved at the refluxing temperature. The amounts of pharmaceutically acceptable salt of escitalopram and solvent used are preferably corresponding to a solvent:solute weight ratio in the range of 0.05:1 to 0.6:1, more preferred 0.1:1 to 0.5:1 and most preferred 0.2:1 to 0.4:1. The solution of escitalopram oxalate is gradually cooled down to the temperature, at which the crystals will be isolated from the mother liquor, in the range of 0–20° C., preferably 0–15° C., and more preferred 7–15° C. maintaining a controlled cooling profile so that the cooling rate in an initial cooling period does not exceed 0.6° C./min, and preferably the cooling rate is kept within the range of 0.2–0.4° C./min, and said initial cooling period extends until the temperature of the crystallisation batch is below 60° C., preferably below 50° C. and more preferred below 40° C., suitably the cooling rate may be kept in this range for the entire cooling. The crystallisation batch is seeded by addition of crystals of escitalopram oxalate at least once during the cooling time in order to avoid excessive supersaturation with respect to escitalopram oxalate and resulting spontaneous crystallisation into small crystalline particles. The seeding is preferably repeated in order to ensure constant presence of crystalline escitalopram oxalate during the cooling, suitably the crystallisation batch is seeded semicontinuously until crystallisation has started. The crystallisation batch is kept at said second temperature for a holding time for crystal growth for at least 1 hour, preferably in the range of 4 to 24 hours and more preferred 6 to 12 hours. After said holding time, the crystalline particles of escitalopram are isolated from the mother liquor using conventional separation techniques, e.g. filtration.

In one embodiment of the invention, the present invention relates to a tablet prepared from a mixture of large crystalline particles of escitalopram oxalate with a median particle size of at least 40 μm, preferably in the range of 50–200 μm and pharmaceutically acceptable excipients. Preferably the tablet is prepared by direct compression.

In another embodiment, the present invention relates to a capsule prepared by filling a mixture of large crystalline particles of escitalopram oxalate with a median particle size of at least 40 μm, preferably in the range of 50–200 μm and pharmaceutically acceptable excipients in a hard gelatine capsule.

Preferably, the solid unit dosage forms according to the invention do not contain a binder.

The solid unit dosage form according to the invention may contain 1–60% w/w active ingredient calculated as

escitalopram base, preferably 4–40% w/w active ingredient calculated as escitalopram base, and more preferred 6–10% w/w active ingredient calculated as escitalopram base. Suitably, the solid unit dosage form of the invention contains 8% w/w active ingredient calculated as escitalopram base.

The solid unit dosage form according to the invention may contain a filler selected from lactose, or other sugars e.g. sorbitol, mannitol, dextrose and sucrose, calcium phosphates (dibasic, tribasic, hydrous and anhydrous), starch, modified starches, microcrystalline cellulose, calcium sulphate and/or calcium carbonate. In a preferred embodiment, the solid unit dosage form of the invention does not contain lactose.

Suitably the filler is a microcrystalline cellulose such as ProSolv SMCC90 manufactured by Penwest Pharmaceuticals or Avicel PH 200 manufactured by FMC Corporation.

Besides the active ingredient and filler, the solid pharmaceutical unit dosage forms may include various other conventional excipients such as disintegrants and optionally minor amounts of lubricants, colorants and sweeteners.

Lubricants used according to the invention may suitably be one or more selected from the group comprising metallic stearates (magnesium, calcium, sodium), stearic acid, wax, hydrogenated vegetable oil, talc and colloidal silica.

Preferably the lubricant is one or more selected from the group comprising talc, magnesium stearate or calcium stearate. Suitably the lubricant is a combination of talc and magnesium stearate. The weight percent of magnesium stearate in the solid unit dosage form is preferably in the range of 0.4% to 2%, and more preferred in the range of 0.7% to 1.4%.

Disintegrants include sodium starch glycolate, croscarmellose, crospovidone, low substituted hydroxypropylcellulose, modified cornstarch, pregelatizined starch and natural starch. Suitably the disintegrant is croscarmellose such Ac-Di-Sol manufactured by FMC.

Optionally the solid, pharmaceutical unit dosage form of the invention may be coated. Suitably the coating is a film coating based on conventional coating mixtures such as Opadry OY-S-28849, white manufactured by Colorcon.

The solid, pharmaceutical unit dosage form of the invention may be prepared by conventional methods using a tablet press with forced feed capability.

The filled, hard gelatine capsule of the invention may be prepared by conventional methods using a capsule filler suitable for powder filling.

In the following, the invention is illustrated by way of examples. However, the examples are merely intended to illustrate the invention and should not be construed as limiting.

EXAMPLE 1

A wet filter cake obtained by precipitation of crude escitalopram oxalate by mixing of ethanolic solutions of escitalopram and oxalic acid, respectively, and containing approximately 35 kg escitalopram oxalate was suspended in 322 L ethanol. The material was dissolved by heating to reflux, and 150 L ethanol was removed by distillation. Cooling was applied, and the mixture was cooled from reflux to 15° C. with a cooling rate between 0.2 and 0.5° C./min in the temperature interval 80 to 40° C. During cooling, the mixture was seeded with escitalopram oxalate at 75, 65 and 60° C. (10 g each time). The crystallisation mixture was kept at 15° C. for 10 hours before the crystalline escitalopram oxalate was isolated. Purified escitalopram oxalate (27.7 kg, 58,2% of theory) was obtained by filtration of the crystallisation mixture, washing with ethanol and drying of the filter cake. Particle size distribution for the resulting escitalopram oxalate is listed in table 1.

TABLE 1

Particle size distribution (Sympatec Helos) for escitalopram oxalate crystals and ProSolv SCMC90

Quantile (%)	Example 1 (μm)	ProSolv SCMC90 (μm)
90	455	291
50	163	130
10	13	37

EXAMPLE 2

Tablet prepared by direct compression of large crystalline particles of escitalopram oxalate.

Tablet ingredients:		
Tablet core		
Escitalopram oxalate	2554 g	(10.2% w/w)
Talc	1400 g	(5.6% w/w)
ProSolv SMCC90	19896 g	(79.6% w/w)
Ac Di Sol	900 g	(3.6%)
Magnesium stearate	250 g	(1.0% w/w)
Film coating		
Opadry OY-S-28849, white	625 g	(2.5% w/w of core weight)

Crystalline particles of escitalopram oxalate from example 1 and talc were sieved through 710 μm screen and blended at 6 rpm for 15 min in a 100 liter Bohle PTM 200 mixer. ProSolv SMCC90 and Ac-Di-Sol were added and blending continued for 15 min. Magnesium stearate was sieved through 710 μm screen and added and blending continued for 3 min.

25 kg of the resulting mixture was tabletted (125.000 tablets/hour) on a Korsch PH 230 tablet press fitted with oblong, embossed, scored 5,5x8 mm punches. Tablet core weight was set to 125 mg. The nominal yield was 200.000 tablets. The tablet press was run until the mixture level was just above the forced feeder, i.e. the tabletting was continued as long as possible in order to identify possible segregation tendencies in the last quantities of mixture. The tablets produced had satisfactory technical properties.

What is claimed is:

1. Crystalline particles of escitalopram oxalate having a median particle size of at least 40 μm.

2. The crystalline particles of claim 1 wherein the median particle size is from 50–200 μm.

3. A method for the manufacture of crystalline particles of escitalopram oxalate, which comprises

(a) dissolving escitalopram oxalate in a solvent at a first temperature between about 50° C. and the refluxing temperature of the solvent to form a solution of escitalopram oxalate;

(b) gradually cooling the solution of escitalopram oxalate to a second temperature between about 0° C. and 20° C. while maintaining a controlled cooling rate;

(c) adding crystals of escitalopram oxalate during the cooling of step (b);

(d) holding the solution at the second temperature; and

(e) isolating crystalline particles of escitalopram oxalate from the solution.

4. The method of claim 3 wherein the median particle size of the crystalline particles is at least 40 μm.

5. The method of claim 3 wherein the median particle size of the crystalline particles is from 50–200 μm.

6. The method of claim 3 wherein the solvent contains at least one alcohol and optionally water.

7. The method of claim 6 wherein the solvent system contains ethanol.

8. The method of claim 3 wherein the solute:solvent weight ratio is between about 0.05:1 and 0.6:1.

9. The method of claim 3 wherein the solute:solvent weight ratio is between about 0.1:1 and 0.5:1.

10. The method of claim 3 wherein the solute:solvent weight ratio is between about 0.2:1 and 0.4:1.

11. The method of claim 3 wherein the first temperature is between about 60° C. and the refluxing temperature of the solvent.

12. The method of claim 3 wherein the first temperature is between about 70° C. and the refluxing temperature of the solvent.

13. The method of claim 3 wherein the second temperature is between about 0° C. and 1520 C.

14. The method of claim 3 wherein the second temperature is between about 7° C. and 15° C.

15. The method of claim 3 wherein the controlled cooling rate comprises an initial cooling period during which the cooling rate does not exceed 0.6° C. per minute.

16. The method of claim 15 wherein the initial cooling period comprises the time between the start of the cooling period and the time at which the temperature is below 60° C.

17. The method of claim 15 wherein the initial cooling period comprises the time between the start of the cooling period and the time at which the temperature is below 50° C.

18. The method of claim 15 wherein the initial cooling period comprises the time between the start of the cooling period and the time at which the temperature is below 40° C.

19. The method of claim 15 wherein the cooling rate of the solution comprises from 0.2 to 0.4° C. per minute.

20. The method of claim 3 which comprises adding crystals of escitalopram oxalate at least two times during the cooling of step (b).

21. The method of claim 3 which comprises holding the solution at the second temperature for at least one hour.

22. The method of claim 3 which comprises holding the solution at the second temperature for 4 to 24 hours.

23. The method of claim 3, which comprises holding the solution at the second temperature for 6 to 12 hours.

24. The method of claim 3, wherein step (e) comprises isolating the crystalline particles of escitalopram oxalate by solid/liquid separation techniques.

25. The method of claim 24, wherein the solid/liquid separation techniques comprise filtration.

26. A solid unit dosage form comprising the crystalline particles of escitalopram oxalate of claim 1.

27. A solid unit dosage form comprising the crystalline particles of escitalopram oxalate of claim 2.

28. The solid unit dosage form of claim 26, which comprises a tablet prepared by direct compression of a mixture of escitalopram oxalate and pharmaceutically acceptable excipients.

29. The solid unit dosage form of claim 28, wherein the tablet is coated.

30. The solid unit dosage form of claim 26, which is prepared by filling a hard gelatin capsule with a mixture of escitalopram oxalate and pharmaceutically acceptable excipients.

31. The solid unit dosage form of claim 26, which does not contain a binder.

32. The solid unit dosage form of claim 26, which comprises 1–30% w/w active ingredient calculated as escitalopram base.

33. The solid unit dosage form of claim 26, which comprises 4–20% w/w active ingredient calculated as escitalopram base.

34. The solid unit dosage form of claim 26, which comprises 6–10% w/w active ingredient calculated as escitalopram base.

35. The solid unit dosage form of claim 26, which further comprises a filler selected from e group consisting of lactose, sugars, calcium phosphates, starch, modified starches, micro crystalline cellulose, calcium sulfate and calcium carbonate.

36. The solid unit dosage form of claim 35, wherein the filler comprises a sugar selected from the group consisting of sorbitol, mannitol, dextrose and sucrose.

37. The solid unit dosage form of claim 35, wherein the filler comprises a calcium phosphate selected from the group consisting of dibasic, tribasic, hydrous and anhydrous calcium phosphate.

38. The solid unit dosage form of claim 35, wherein the filler comprises microcrystalline cellulose.

39. The solid unit dosage form of claim 38, wherein the microcrystalline cellulose is selected from the group consisting of ProSolv SMCC90 and Avicel PH 200.

40. The solid unit dosage form of claim 26, further comprising a lubricant.

41. The solid unit dosage form of claim 40, wherein the lubricant comprises a member selected from the group consisting of metallic stearates, stearic acid, wax, hydrogenated vegetable oil, talc and colloidal silica.

42. The solid unit dosage form of claim 41, wherein the lubricant comprises a metallic stearate selected from the group consisting of magnesium, calcium and sodium stearate.

43. The solid unit dosage form of claim 41, wherein the lubricant comprises a member selected from the group consisting of talc, magnesium stearate and calcium stearate.

44. The solid unit dosage form of claim 41, wherein the lubricant comprises talc and magnesium stearate.

45. The solid unit dosage form of claim 44, wherein the magnesium stearate is present in a weight percent of 0.4% to 2%, calculated on the weight of the solid dosage form.

46. The solid unit dosage form of claim 44, wherein the magnesium stearate is present in a weight percent of 0.7% to 1.4%, calculated on the weight of the solid dosage form.

47. The solid unit dosage form of claim 26, which is substantially free of lactose.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,916,941 B2
DATED : July 12, 2005
INVENTOR(S) : Troels V. Christensen et al.

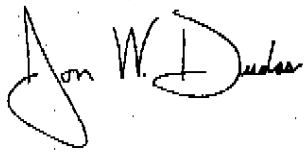
It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 7,
Line 24, please delete "1520 C" and substitute -- 15º C -- therefor.

Column 8,
Line 20, please delete "from c group" and substitute -- from the group -- therefor.
Line 22, please delete "micro crystalline" and substitute -- microcrystalline -- therefor.

Signed and Sealed this

Thirtieth Day of August, 2005



JON W. DUDAS
*Director of the United States Patent **and** Trademark Office*

CIVIL COVER SHEET

County in which this action arose: Wayne

...ivil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as ...by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose ...iating the civil docket sheet. (SEE INSTRUCTIONS ON THE REVERSE OF THE FORM.)

I. (a) PLAINTIFFS

CARACO PHARMACEUTICAL LABORATORIES, LTD.

DEFENDANTS

FOREST LABORATORIES, INC., FOREST LABORATORIES HOLDINGS, LTD. and H. LUNDBECK A/S

(b) County of Residence of First Listed Plaintiff: Wayne
(EXCEPT IN U.S. PLAINTIFF CASES)

County of Residence of First Listed Defendant
(IN U.S. PLAINTIFF CASES ONLY)

NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE LAND INVOLVED.

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Attorneys (If Known)

II. BASIS OF JURISDICTION (Select One Box Only)

- ☐ 1 U.S. Government Plaintiff
- ☒ 3 Federal Question (U.S. Government Not a Party)
- ☐ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in Item III)

III. CITIZENSHIP OF PRINCIPAL PARTIES (Select One Box for Plaintiff and One Box for Defendant)
(For Diversity Cases Only)

	PTF	DEF		PTF	DEF
Citizen of This State	☐ 1	☐ 1	Incorporated ...	☒ 4	☐ 4
	☐ 5	☒ 5			
	☐ 6	☐ 6			

Case: 4:07-cv-10737
Assigned To: Gadola, Paul V
Referral Judge: Scheer, Donald A
Filed: 02-20-2007 At 03:21 PM
CMP CARACO PHARMACEEUTICAL VS FORES T LAB ET AL (LE)

IV. NATURE OF SUIT (Select One Box Only)

CONTRACT
- ☐ 110 Insurance
- ☐ 120 Marine
- ☐ 130 Miller Act
- ☐ 140 Negotiable Instrument
- ☐ 150 Recovery of Overpayment & Enforcement of Judgment
- ☐ 151 Medicare Act
- ☐ 152 Recovery of Defaulted Student Loans (Excl. Veterans)
- ☐ 153 Recovery of Overpayment of Veteran's Benefits
- ☐ 160 Stockholders' Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability
- ☐ 196 Franchise

TORTS

PERSONAL INJURY
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers' Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury

PERSONAL INJU
- ☐ 362 Personal Injury - Med. Malpractice
- ☐ 365 Personal Injury - Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☐ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

REAL PROPERTY
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

CIVIL RIGHTS
- ☐ 441 Voting
- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 444 Welfare
- ☐ 445 Amer. w/Disabilities - Employment
- ☐ 446 Amer. w/Disabilities - Other
- ☐ 440 Other Civil Rights

PRISONER PETITIONS
- ☐ 510 Motions to Vacate Sentence
- Habeas Corpus:
- ☐ 530 General
- ☐ 535 Death Penalty
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition

830

- ☐ 620 Other Food & Drug
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 630 Liquor Laws
- ☐ 640 R.R. & Truck
- ☐ 650 Airline Regs.
- ☐ 660 Occupational Safety/Health
- ☐ 690 Other

LABOR
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor/Mgmt. Relations
- ☐ 730 Labor/Mgmt.Reporting & Disclosure Act
- ☐ 740 Railway Labor Act
- ☐ 790 Other Labor Litigation
- ☐ 791 Empl. Ret. Inc. Security Act

- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ☐ 820 Copyrights
- ☒ 830 Patent
- ☐ 840 Trademark

SOCIAL SECURITY
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWC/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

FEDERAL TAX SUITS
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS—Third Party 26 USC 7609

OTHER STATUTES
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced and Corrupt Organizations
- ☐ 480 Consumer Credit
- ☐ 490 Cable/Sat TV
- ☐ 810 Selective Service
- ☐ 850 Securities/Commodities/ Exchange
- ☐ 875 Customer Challenge 12 USC 3410
- ☐ 890 Other Statutory Actions
- ☐ 891 Agricultural Acts
- ☐ 892 Economic Stabilization Act
- ☐ 893 Environmental Matters
- ☐ 894 Energy Allocation Act
- ☐ 895 Freedom of Information Act
- ☐ 900 Appeal of Fee Determination Under Access to Justice
- ☐ 950 Constitutionality of State Statutes

V. ORIGIN (Select One Box Only)

☒ 1 Original Proceeding ☐ 2 Removed from State Court ☐ 3 Remanded from Appellate Court ☐ 4 Reinstated or Reopened ☐ 5 Transferred from another district (specify) ☐ 6 Multidistrict Litigation ☐ 7 Appeal to District Judge from Magistrate Judgment

VI. CAUSE OF ACTION

Cite the U.S. Civil Statute under which you are filing (Do not cite jurisdictional statutes unless diversity):
35 USC 271

Brief description of cause:
Declaratory judgment for non-infringement of patent

VII. REQUESTED IN COMPLAINT:

☐ CHECK IF THIS IS A CLASS ACTION UNDER F.R.C.P. 23

DEMAND $

CHECK YES only if demanded in complaint:
JURY DEMAND: ☐ Yes ☒ No

VIII. RELATED CASE(S) IF ANY (See instructions): JUDGE Bernard A. Friedman DOCKET NUMBER 2:06-cv-13143

DATE 2/20/07

SIGNATURE OF ATTORNEY OF RECORD

FOR OFFICE USE ONLY

RECEIPT # AMOUNT APPLYING IFP JUDGE MAG. JUDGE

[redacted]UANT TO LOCAL RULE 83.11

1. Is this a case that has been previously dismissed? ☐ Yes ☒ No

If yes, give the following information:

Court: _____

Case No.: _____

Judge: _____

2. Other than stated above, are there any pending or previously discontinued or dismissed companion cases in this or any other court, including state court? (Companion cases are matters in which it appears substantially similar evidence will be offered or the same or related parties are present and the cases arise out of the same transaction or occurrence.) ☒ Yes ☐ No

If yes, give the following information:

Court: USDC E.D. Michigan

Case No.: 2:06-cv-13143

Judge: Bernard A. Friedman

Notes : Same

As identified in Section VIII on page 1 of the Civil Cover Sheet, there is currently a companion case pending in the United States District Court for the Eastern District of Michigan. Forest Laboratories, Inc., et al. v. Caraco Pharmaceutical Laboratories, Ltd., Case No. 2:06-cv-13143.