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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

CELGENE CORPORATION, NOVARTIS PHARMACEUTICALS CORPORATION and NOVARTIS PHARMA AG, Plaintiffs, v. TEVA PHARMACEUTICALS USA, INC., Defendant.	Civil Action No. 04 - 4030 (SRC) **COMPLAINT**

Plaintiffs Celgene Corporation ("Celgene") and Novartis Pharmaceuticals Corporation and Novartis Pharma AG (collectively referred to herein as "Novartis"), by their attorneys, for their Complaint against Teva Pharmaceuticals USA, Inc. ("Teva"), allege as follows:

Nature of the Action

1. This is an action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 100 *et seq.*, and, more particularly, 35 U.S.C. §§ 271(e)(2) and 281. The act of infringement is Teva's filing of an Abbreviated New Drug Application ("ANDA"), and amendments thereto, with the United States Food and Drug Administration ("FDA") in

which Teva seeks approval to market a generic version of Novartis's patented FOCALIN™ drug product prior to the expiration of various United States Patents owned by Celgene.

The Parties

2. Celgene Corporation is a corporation organized and existing under the laws of the State of Delaware, and has a principal place of business at 7 Powder Horn Drive, Warren, NJ 07059.

3. Novartis Pharmaceuticals Corporation is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 59 Route 10, East Hanover, New Jersey 07936.

4. Novartis Pharma AG is a corporation organized and existing under the laws of Switzerland, having an office and place of business at Lichtstrasse 35, CH-4056 Basel, Switzerland.

5. Teva Pharmaceuticals USA, Inc. is a corporation organized and existing under the laws of the Delaware, having a principal place of business at 1090 Horsham Road, P.O. Box 1090, North Wales, PA 19454-1090.

Jurisdiction and Venue

6. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

7. This Court has personal jurisdiction over Teva by virtue of, *inter alia*, Teva's continuous and systematic contacts with New Jersey, its sale of prescription drugs in New Jersey, its registration of prescription drugs in the *New Jersey Generic Formulary* of the New Jersey Department of Health and Senior Services, its consent to being sued in New Jersey, as evidenced by its registration to do business in New Jersey and its appointment of a registered agent in New

Jersey, its regular and established places of business at 92 Route 46 East, Elmwood Park, New Jersey and at 8/10 Gloria Lane, Fairfield, New Jersey, and its performance of tortious acts that will result in foreseeable harm in New Jersey.

8. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391 and 1400(b).

The Patent In Suit and the FOCALIN™ Drug Product

9. United States Patent No. 5,908,850 ("the '850 patent"), entitled "Method of Treating Attention Deficit Disorders With D-Threo Methylphenidate," duly and legally issued to Celgene on June 1, 1999, naming as inventors Andrew L. Zeitlin *et al.*, by the United States Patent and Trademark Office. A copy of the '850 patent is attached hereto as Exhibit A. The '850 patent claims are directed to methods of treatment using *d-threo* methylphenidate.

10. Celgene is the owner by assignment of all right, title and interest in the '850 patent. Novartis Pharma AG is the exclusive licensee of the '850 patent.

11. Novartis Pharmaceuticals Corporation holds an approved New Drug Application for tablets of 2.5 mg, 5 mg and 10 mg of the hydrochloride salt of *d-threo* methylphenidate, also known as dexmethylphenidate hydrochloride, which it sells as a commercial product under the trade name FOCALIN™. The approved use of the commercial products is covered by the '850 patent.

Acts Giving Rise To This Action

12. On or about July 9, 2004, plaintiffs received a letter from Teva notifying them that Teva had filed a patent certification pursuant to section 505(j)(2) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(j)(2), directed to dexmethylphenidate hydrochloride. In the

letter, Teva stated that it had submitted ANDA No. 77-107 to the FDA seeking marketing approval for dexmethylphenidate hydrochloride tablets, 5 mg and 10 mg.

13. On or about July 28, 2004, plaintiffs received a second letter from Teva regarding ANDA No. 77-107 (the July 9th and July 28th letters are jointly referred to herein as "the Notification Letters"). In this second letter, Teva notified the plaintiffs that Teva had filed an amendment to ANDA No. 77-107 seeking marketing approval for dexmethylphenidate hydrochloride tablets, 2.5 mg (the 2.5 mg, 5 mg and 10 mg tablets are collectively referred to herein as "Teva's dexmethylphenidate hydrochloride tablets").

14. Teva submitted its ANDA to obtain FDA approval to engage in the commercial manufacture, use and sale of dexmethylphenidate hydrochloride tablets prior to the expiration of the '850 patent, which is listed in the FDA publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" as being applicable to the FOCALIN™ products. On information and belief, Teva intends to engage and will engage in the commercial manufacture, use and sale of dexmethylphenidate hydrochloride tablets promptly upon receiving FDA approval to do so.

15. The Notification Letters state that Teva's ANDA No. 77-107 contained a "Paragraph IV Certification" that, in Teva's opinion, the '850 patent is invalid.

16. The Notification Letters state no grounds for unenforceability of the '850 patent, or for non-infringement of that patent by Teva's proposed marketing of the dexamethylphenidate hydrochloride tablets.

17. Upon information and belief, Teva's ANDA No. 77-107 contains information showing that dexmethylphenidate hydrochloride tablets (a) are bioequivalent to the patented FOCALIN™ products, (b) have the same active ingredient as the patented FOCALIN™

products, (c) have the same route of administration, dosage form and strength as the patented FOCALIN™ products, and (d) have the same, or substantially the same, proposed labeling, and the same indication and usage as the patented FOCALIN™ products.

18. This action is being brought pursuant to 21 U.S.C. § 355(j)(5)(B)(iii) before the expiration of forty-five days from the date of receipt of Teva's July 9, 2004 letter.

Count I: Infringement of the '850 Patent

19. Plaintiffs repeat and reallege the allegations of paragraphs 1-18 as though fully set forth herein.

20. Teva's submission of its ANDA to obtain approval to engage in the commercial manufacture, use and sale of dexmethylphenidate hydrochloride tablets, prior to the expiration of the '850 patent, constitutes infringement of one or more of the claims of that patent under 35 U.S.C. § 271(e)(2).

21. Unless enjoined by this Court, Teva, upon FDA approval of Teva's ANDA, will infringe the '850 patent under 35 U.S.C. § 271 by making, using, offering to sell, importing, or selling dexmethylphenidate hydrochloride tablets in the United States.

22. Teva had notice of the '850 patent beginning prior to undertaking its act of infringement. Teva's infringement has been, and continues to be, willful and deliberate.

23. Plaintiffs will be substantially and irreparably damaged and harmed if Teva's infringement is not enjoined. Plaintiffs do not have an adequate remedy at law.

Prayer For Relief

WHEREFORE, plaintiffs respectfully request the following relief:

(A) A judgment declaring that Teva has infringed, and that Teva's making, using, selling, offering to sell or importing of dexmethylphenidate hydrochloride tablets will infringe

the '850 patent;

(B) A judgment ordering that the effective date of any FDA approval for Teva to market dexmethylphenidate hydrochloride tablets, or any other drug product containing dexmethylphenidate hydrochloride, be no earlier than the date on which the '850 patent expires;

(C) A judgment permanently enjoining Teva from making, using, selling, offering to sell, or importing dexmethylphenidate hydrochloride tablets until after the expiration of the '850 patent;

(D) A declaration that the commercial manufacture, use, importation into the United States, sale or offering for sale of Teva's dexmethylphenidate hydrochloride tablets will infringe the '850 patent;

(E) A declaration that the commercial manufacture, use, importation into the United States, sale or offering for sale of Teva's dexmethylphenidate hydrochloride tablets will induce and/or contribute to infringement of '850 patent.

(F) If Teva engages in the commercial manufacture, use, importation into the United States, offer to sell, or sale of dexmethylphenidate hydrochloride tablets prior to the expiration of the '850 patent, a judgment awarding damages to plaintiffs resulting from such infringement, increased to treble the amount found or assessed, together with interest;

(G) Attorneys' fees in this action pursuant to 35 U.S.C. § 285;

(H) Costs and expenses in this action; and

(I) Such further and other relief as this Court may deem just and proper.

Dated: August 19, 2004

By: _____

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US005908850A

United States Patent [19]

Zeitlin et al.

[11] Patent Number: 5,908,850

[45] Date of Patent: Jun. 1, 1999

[54] **METHOD OF TREATING ATTENTION DEFICIT DISORDERS WITH D-THREO METHYLPHENIDATE**

[75] Inventors: **Andrew L. Zeitlin**, Millington; **Maghsoud M. Dariani**, Fanwood; **David I. Stirling**, Branchburg, all of N.J.

[73] Assignee: **Celgene Corporation**, Warren, N.J.

[21] Appl. No.: **08/827,230**

[22] Filed: **Apr. 2, 1997**

Related U.S. Application Data

[63] Continuation of application No. 08/567,131, Dec. 4, 1995, abandoned.

[51] **Int. Cl.**[6] **A61K 31/445**

[52] **U.S. Cl.** **514/315**

[58] **Field of Search** 514/315

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WO 97/03672	2/1997	WIPO .
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Primary Examiner—Raymond Henley, III

Attorney, Agent, or Firm—Woodcock Washburn Kurtz Mackiewicz & Norris LLP

[57] **ABSTRACT**

Methods for treating Attention Deficit Disorder, Attention Deficit Hyperactivity Disorder, AIDS Dementia Complex and cognitive decline in HIV-AIDS while minimizing drug hypersensitivity, toxicity, side effects, euphoric effect, and drug abuse potential by administration of d-threo-methylphenidate or pharmaceutically acceptable salts thereof.

4 Claims, No Drawings

METHOD OF TREATING ATTENTION DEFICIT DISORDERS WITH D-THREO METHYLPHENIDATE

This is a continuation of application Ser. No. 08/567,131, filed Dec. 4, 1995, now abandoned, disclosure of which is herein incorporated by reference.

The present invention relates to methods of treating certain Central Nervous System disorders such as Attention Deficit Disorder (ADD), Attention Deficit Hyperactivity Disorder (ADHD), HIV/AIDS cognitive decline, and AIDS Dementia Complex with decreased side effects, reduced euphoric effect, and reduced drug abuse potential.

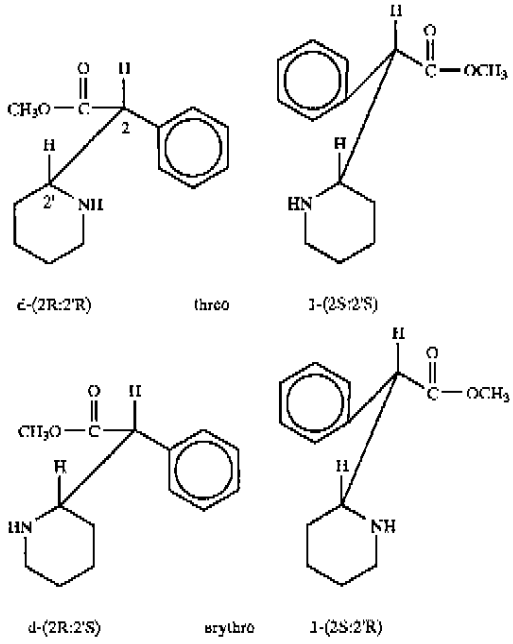
BACKGROUND OF THE INVENTION

Attention Deficit Disorder (ADD) is the most commonly diagnosed illness in children. Patrick et al., *J. Pharmacol. & Exp. Therap.*, 241:152–158 (1987). Symptoms of ADD include distractibility and impulsivity. A related disorder, termed Attention Deficit Hyperactivity Disorder (ADHD), is further characterized by increased symptoms of hyperactivity in patients. Racemic methylphenidate (e.g., Ritalin®) is a mild Central Nervous System stimulant with pharmacological activity qualitatively similar to amphetamines, and has been the drug of choice for symptomatic treatment of ADD in children. Greenhill, L., *Child & Adol. Psych. Clin. N.A.*, Vol. 4, Number 1:123–165 (1995). Current administration of racemic methylphenidate, however, results in notable side effects such as anorexia, weight loss, insomnia, dizziness and dysphoria. Additionally, racemic methylphenidate which is a Schedule II controlled substance, produces a euphoric effect when administered intravenously or through inhalation, and thus carries a high potential for substance abuse in patients.

At least 70% of HIV-infected individuals who have developed Acquired Immunodeficiency Syndrome (AIDS) eventually manifest cognitive defects, and many display signs and symptoms of dementia. See Navia et al., *Annals of Neurology*, 19:517–524 (1986). Complaints of forgetfulness, loss of concentration, fatigue, depression, loss of attentiveness, mood swings, personality change, and thought disturbance are common in patients with Human Immunodeficiency Virus (HIV) disease. Douzenis et al., *Proc. 7th Int'l. Conf. AIDS*, 1, MB, 2135:215 (1991); Holmes et al., *J. Clin. Psychiatry*, 50:5–8 (1989). Racemic methylphenidate has been used to treat cognitive decline in AIDS/ARC patients. Brown, G., *Intl. J. Psych. Med.* 25(1): 21–37 (1995). As described above, racemic methylphenidate which is a Schedule II controlled substance, produces a euphoric effect when administered intravenously or through inhalation, and thus carries a high potential for drug abuse in AIDS patients.

Glutathione is an important antioxidative agent that protects the body against electrophilic reactive compounds and intracellular oxidants. It has been postulated that HIV-AIDS patients suffer from drug hypersensitivity due to drug overload and an acquired glutathione deficiency. See Uetrecht et al., *Pharmacol. Res.*, 6:265–273 (1989). Patients with HIV infection have demonstrated a reduced concentration of glutathione in plasma, cells and broncho-alveolar lavage fluid. Staal et al., *Lancet*, 339:909–912 (1992). Clinical data suggests that HIV-seropositive individuals display adverse reactions to the simultaneous administration of several otherwise therapeutic drugs. Rieder et al., *Ann. Intern. Med.*, 110:286–289 (1989). It is therefore desirable to provide for the administration of methylphenidate in reduced dosages among patients with drug hypersensitivity due to HIV infection.

Methylphenidate possesses two centers of chirality and thus can exist as four separate optical isomers. The four isomers of methylphenidate are as follows:



Diastereomers are known in the art to possess differing physical properties, such as melting point and boiling point. For example, while the threo- racemate of methylphenidate produces the desired Central Nervous System action, the erythro- racemate contributes to hypertensive side effects and exhibits lethality in rats.

Additional studies in animals, children and adults have demonstrated pharmacological activity in the d-threo isomer of methylphenidate (2R:2'R) . See Patrick et al., *J. Pharmacol. & Exp. Therap.*, 241:152–158 (1987). Although the role of the l-isomer in toxicity or adverse side effects has not been thoroughly examined, the potential for isomer ballast in methylphenidate is of concern for many patient groups, particularly those drug hypersensitive patients as described above.

Although l-threo-methylphenidate is rapidly and stereoselectively metabolized upon oral administration, intravenous administration or inhalation results in high l-threo-methylphenidate serum levels. Srinivas et al., *Pharmacol. Res.*, 10:14–21 (1993). Intravenous administration and inhalation are the methods of choice by drug abusers of current methylphenidate formulations. The present invention postulates that the euphoric effect produced by current formulations of methylphenidate is due to the action of l-threo-methylphenidate.

Accordingly, it has been discovered that the use of the d-threo isomer (2R:2'R) of methylphenidate, substantially free of the l-threo isomer produces a methylphenidate medication which retains high activity levels and simultaneously possesses reduced euphoric effect and reduced potential for abuse among patients.

U.S. Pat. No. 2,507,631, to Hartmann et al. describes methylphenidate and processes for making the same.

U.S. Pat. No. 2,957,880, to Rometsch et al. describes the conversion of α-aryl-α-piperidyl-(2)-acetic acids and

derivatives thereof (including methylphenidate) into their respective racemates.

Holmes et al., *J. Clin. Psychiatry,* 50:5–8 (1989) reported on the use of racemic methylphenidate (Ritaline®) and dextroamphetamines in the treatment of cognitive impairment in AIDS patients.

Srinivas et al., *J. Pharmacol. & Exp. Therap.,* 241:300–306 (1987) described use of racemic dl-threo-methylphenidate (Ritalin®) in the treatment of ADD in children. This study noted a 5-fold increase in plasma levels of d-threo-methylphenidate in children treated with racemic methylphenidate, but was otherwise inconclusive with regard to the efficacy of a single methylphenidate isomer at therapeutically significant doses.

Srinivas et al., *Clin. Pharmacol. Ther.,* 52:561–568 (1992) studied the administration of dl-threo, d-threo and l-threo-methylphenidate to children suffering from ADHD. While Srinivas et al. reported the pharmacodynamic activity of dl-threo-methylphenidate resides in the d-threo isomer, this study investigated neither the adverse side effects of the l-threo isomer, nor the euphoric effects of the single isomers or racemate. Single isomer dosages below ½ of the racemate dosage were not studied.

Patrick et al., *J. Pharmacol. & Exp. Therap.,* 241:152–158 (1986) examined the pharmacology of the enantiomers of threo-methylphenidate, and assessed the relative contribution of each isomer to central and peripheral actions of Ritalin®.

Brown, G., *Intl. J. Psych. Med.,* 25(1):21–37 (1995) reported the use of racemic methylphenidate for the treatment of AIDS cognitive decline.

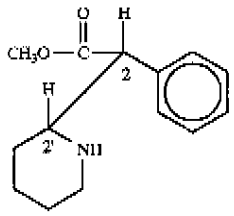
Patrick et al., *Psychopharmacology: The Third Generation of Progress,* Raven Press, N.Y. (1987) examined the pharmacokinetics and actions of methylphenidate in the treatment of Attention Deficit Hyperactivity Disorder (ADHD). Patrick noted the d-threo isomer possesses higher activity than the l-threo isomer, and that d-threo methylphenidate may be responsible for the therapeutic activity in the racemic drug.

Aoyama et al., *Clin. Pharmacol. Ther.,* 55:270–276 (1994) reported on the use of (+)-threo-methylphenidate in the treatment of hypersomnia. Aoyama et al. describe a correlation between sleep latency in patients and plasma concentration or (+)-threo-methylphenidate.

SUMMARY OF THE INVENTION

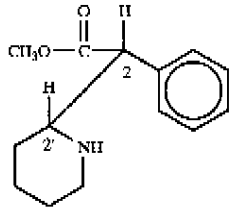
The present invention is based on the discovery that d-threo-methylphenidate (2R:2'R) possesses enhanced therapeutic activity with reduced side effects, and l-threo-methylphenidate produces undesirable side effects, euphoria and drug abuse potential in patients suffering from Attention Deficit Disorder, Attention Deficit Hyperactivity Disorder, AIDS cognitive decline, and AIDS Dementia Complex.

The present invention thus relates to methods of treating Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder in children and adults while providing for reduced side effects, reduced euphoric effect and reduced potential for abuse potential through administration of d-threo-methylphenidate (2R:2'R) of the formula:



or a pharmaceutically acceptable salt thereof, substantially free of the l-threo isomer.

The invention further relates to methods of treating AIDS-related dementia and related cognitive disorders while providing for reduced side effects, reduced euphoric effect, and reduced abuse potential through administration of d-threo-methylphenidate (2R:2'R) of the formula:



or a pharmaceutically acceptable salt thereof, substantially free of the l-threo isomer.

Prescription of methylphenidate to treat AIDS cognitive decline and AIDS Dementia Complex associated with HIV infection is becoming increasingly popular. However, high doses in excess of 40 mg/day are not well tolerated by a substantial number of HIV-infected patients when treated over weeks or months. Brown, G., *Int'l J. Psychiatry. Med.,* 25:21–37 (1995). The d-threo isomer use of the present invention thus enables a lowered dosing therapy resulting in improved efficacy for diseased patients and particularly HIV-infected patients.

Moreover, administration of the d-threo isomer to patients will result in decreased side effects, reduced euphoric effect, and substantially reduce the potential for abuse of the product.

DETAILED DESCRIPTION OF THE INVENTION

Racemic methylphenidate and its individual isomers are known. See U.S. Pat. Nos. 2,507,631 and 2,957,880. They can be prepared by conventional techniques, and can be obtained from a variety of commercial sources.

The d-threo isomer of the present invention can be administered orally, rectally, parenterally, or transdermally, alone or in combination with other psychostimulants, antidepressants, and the like to a patient in need of treatment. Oral dosage forms include tablets, capsules, dragees, and similar shaped compressed pharmaceutical forms. Isotonic saline solutions containing 20–100 milligrams/milliliter can be used for parenteral administration which includes intramuscular, intrathecal, intravenous and intra-arterial routes of administration. Rectal administration can be effected through the use of suppositories formulated from conventional carriers such as cocoa butter. Transdermal administration can be effected through the use of transdermal patch delivery systems and the like. The preferred routes of administration are oral and parenteral.

The dosage employed must be carefully titrated to the patient, considering age, weight, severity of the condition, and clinical-profile. Typically, the amount of d-threo-methylphenidate administered will be in the range of 5–50 mg/day, but the actual decision as to dosage must be made by the attending physician.

The present invention provides enhanced relief for patients suffering from Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder while providing for reduced side effects, reduced euphoric effect, and reduced abuse potential through administration of d-threo-methylphenidate substantially free of the l-threo isomer.

The invention further provides for treatment of AIDS-related dementia and related cognitive disorders with d-threo-methylphenidate substantially free of the l-threo isomer while providing for reduced side effects, reduced euphoric effect, and reduced abuse potential.

The term, "substantially free of the l-threo-isomer" means that the composition contains at least 90% by weight of d-threo-methylphenidate, and 10% by weight of l-threo-methylphenidate. In the most preferred embodiment, the term "substantially free of the l-threo isomer" means that the composition contains at least 99% by weight of d-threo-methylphenidate and 1% or less of l-threo-methylphenidate.

The following examples will serve to further typify the nature of the invention, but should not be construed as a limitation on the scope thereof, which is defined solely by the appended claims.

EXAMPLE 1

Tablets for chewing, each containing 5 milligrams of d-threo-methylphenidate, can be prepared in the following manner:

Composition (for 1000 tablets)	
d-threo-methylphenidate	5.00 grams
mannitol	15.33 grams
lactose	10.00 grams
talc	1.40 grams
glycine	0.83 grams
stearic acid	0.66 grams
saccharin	0.10 grams
5% gelatin solution q.s.	

All the solid ingredients are first forced through a sieve of 0.25 mm mesh width. The mannitol and the lactose are mixed, granulated with the addition of gelatin solution, forced through a sieve of 2 mm mesh width, dried at 50° C. and again forced through a sieve of 1.7 mm mesh width. The d-threo-methylphenidate, the glycine and the saccharin are carefully mixed, the mannitol, the lactose granulate, the stearic acid and the talc are added and the whole is mixed thoroughly and compressed to form tablets of approximately 10 mm diameter which are concave on both sides and have a breaking groove on the upper side.

EXAMPLE 2

Tablets, each containing 10 milligrams of d-threo-methylphenidate, can be prepared in the following manner:

Composition (for 1000 tablets)	
d-threo-methylphenidate	10.0 grams
lactose	328.5 grams
corn starch	17.5 grams
polyethylene glycol 6000	5.0 grams
talc	25.0 grams
magnesium stearate	4.0 grams
demineralized water q.s.	

The solid ingredients are first forced through a sieve of 0.6 mm mesh width. Then the d-threo-methylphenidate, lactose, talc, magnesium stearate and half of the starch are intimately mixed. The other half of the starch is suspended in 65 milliliters of water and this suspension is added to a boiling solution of the polyethylene glycol in 260 milliliters of water. The resulting paste is added to the pulverulent substances, and the whole is mixed and granulated, if necessary with the addition of water. The granulate is dried overnight at 35° C., forced through a sieve of 1.2 mm mesh width and compressed to form tablets of approximately 10 mm diameter which are concave on both sides and have a breaking notch on the upper side.

EXAMPLE 3

Gelatin dry-filled capsules, each containing 20 milligrams of d-threo-methylphenidate, can be prepared in the following manner:

Composition (for 1000 capsules)	
d-threo-methylphenidate	20.0 grams
microcrystalline cellulose	6.0 grams
sodium lauryl sulfate	0.4 grams
magnesium stearate	1.6 grams

The sodium lauryl sulfate is sieved into the d-threo-methylphenidate through a sieve of 0.2 mm mesh width and the two components are intimately mixed for 10 minutes. The microcrystalline cellulose is then added through a sieve of 0.9 mm mesh width and the whole is again intimately mixed for 10 minutes. Finally, the magnesium stearate is added through a sieve of 0.8 mm width and, after mixing for a further 3 minutes, the mixture is introduced in portions of 28 milligrams each into size 0 (elongated) gelatin dry-fill capsules.

EXAMPLE 4

A 0.2% injection or infusion solution can be prepared, for example, in the following manner:

d-threo-methylphenidate	5.0 grams
sodium chloride	22.5 grams
phosphate buffer pH 7.4	300.0 grams
demineralized water to 2500 mL	

The d-threo-methylphenidate is dissolved in 1000 milliliters of water and filtered through a microfilter or slurried in 1000 mL of H_2O. The buffer solution is added and the whole is made up to 2500 milliliters with water. To prepare dosage unit forms, portions of 1.0 or 2.5 milliliters each are introduced into glass ampoules (each containing respectively 2.0 or 5.0 milligrams of d-threo-methylphenidate).

What is claimed is:

1. A method of treating at least one of Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder and

providing enhanced therapeutic activity, reduced side effects euphoric effect, or potential for drug abuse as compared to racemic threo methylphenidate, said method comprising administering to a human exhibiting symptoms of such disorder therapeutically effective amounts of D-threo methylphenidate or pharmaceutically acceptable salt thereof, substantially free of L-threo methylphenidate, on a daily basis.

2. The method according to claim 1 wherein the amount administered is 5 mg to 50 mg per day.

3. The method according to claim 1 wherein the amount of d-threo-methylphenidate or a pharmaceutically acceptable salt thereof is greater than 99% by weight.

4. The method according to claim 1 wherein said D-threo methylphenidate is administered together with a pharmaceutically acceptable carrier.

* * * * *

FED. R. CIV. P. 7.1 DISCLOSURE STATEMENT

Pursuant to Rule 7.1 of the Fed. R. Civ. P., counsel for Plaintiffs Celgene Corporation, Novartis Pharmaceuticals Corporation and Novartis Pharma AG certifies the following:

1. The full name of each party represented by me is:

   a) Celgene Corporation;
   b) Novartis Pharmaceuticals Corporation;
   c) Novartis Pharma AG;

2. There are no corporate parents of Celgene Corporation which are publicly held, other than Celgene Corporation itself. No publicly held company owns 10% or more of Celgene Corporation's stock.

3. Novartis AG, a publicly held corporation, is the parent company of Novartis Pharmaceuticals Corporation. Novartis AG is the only publicly held company that directly or indirectly owns 10% or more of Novartis Pharmaceuticals Corporation's stock.

4. Novartis AG, a publicly held corporation, is the parent company of Novartis Pharma AG. Novartis AG is the only publicly held company that directly or indirectly owns 10% or more of Novartis Pharma AG's stock.

5. There are no corporate parents of Novartis AG which are publicly held, other than Novartis AG itself. No publicly held company owns 10% or more of Novartis AG's stock.

Dated: August 19, 2004

Charles M. Lizza (CL 5036)

LOCAL CIVIL RULE 11.2 CERTIFICATION

I hereby certify that the matter in controversy is not the subject of any other action pending in any court, or of any pending arbitration or administrative proceeding.

Dated: August 19, 2004

Charles M. Lizza (CL 5036)