IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ACTAVIS ELIZABETH LLC, Plaintiff, v. CHARLES E. JOHNSON, Acting Secretary of Health and Human Services, 200 Independence Avenue, S.W. Washington, D.C. 20201, FRANK M. TORTI, Acting Commissioner of Food and Drugs, 200 C Street, S.W. Washington, D.C. 20201 and UNITED STATES FOOD AND DRUG ADMINISTRATION, 5600 Fishers Lane Rockville, MD 20857, Defendants.	Civil Action No. ___-_____

COMPLAINT

Plaintiff Actavis Elizabeth LLC ("Actavis"), for its complaint against the defendants, Charles E. Johnson, Acting Secretary of Health and Human Services, and Frank M. Torti, Acting Commissioner of Food and Drugs, United States Food and Drug Administration and the United States Food and Drug Administration (collectively "FDA"), alleges as follows:

NATURE OF THE ACTION

1. On January 28, 2009, Actavis filed an Abbreviated New Drug Application ("ANDA") under the generic drug provisions of the Federal Food, Drug and Cosmetic Act ("FDCA"), seeking FDA approval to market generic lisdexamfetamine dimesylate capsules 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg. Such drug product is currently marketed by Shire Development, Inc. and/or Shire U.S., Inc. (collectively "Shire") under the trade name Vyvanse®.

2. On or about February 23, 2007, FDA approved Shire's New Drug Application ("NDA") for Vyvanse and erroneously granted new chemical entity ("NCE") exclusivity to Vyvanse.

3. The NCE exclusivity period for Vyvanse is set to expire on February 23, 2012. Under FDA's erroneous award of NCE exclusivity to Vyvanse, FDA has taken the position that no ANDA directed to Vyvanse may be filed with FDA until that time, unless the ANDA contains a "Paragraph IV" certification, in which case it may be submitted one year prior to February 23, 2012. Actavis' ANDA contains a Paragraph IV certification.

4. The FDA-identified active ingredient in Vyvanse, lisdexamfetamine dimesylate, is a covalent derivative of dextroamphetamine. According to the Vyvanse product insert, lisdexamfetamine "is a prodrug of dextroamphetamine. After oral administration, lisdexamfetamine is rapidly absorbed in the digestive tract and converted to dextroamphetamine, which is responsible for the drug's activity." (Exhibit A, Vyvanse Product Insert.)

5. FDA refused to file Actavis' ANDA and returned it to Actavis, stating that FDA could not review or possess Actavis' ANDA while the NCE exclusivity was still in effect.

6. As set forth more fully herein, FDA's grant of NCE exclusivity to Vyvanse and FDA's refusal to file Actavis' ANDA is arbitrary, capricious and contrary to law, and it has caused, and continues to cause, Actavis harm for which Actavis is entitled to declaratory and injunctive relief, including but not limited to:

a. Issuance of judgment declaring that FDA's grant of NCE exclusivity to Vyvanse is arbitrary, capricious and contrary to law;

b. Issuance of a judgment declaring that FDA's refusal to file Actavis' ANDA is arbitrary, capricious and contrary to law; and

c. Issuance of an injunction directing FDA to rescind the NCE exclusivity for Vyvanse and directing FDA to accept the Actavis ANDA with an effective filing date of January 28, 2009 in order to place Actavis in the position it would have been in but for FDA's unlawful action.

THE PARTIES

7. Plaintiff Actavis is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business in Elizabeth, New Jersey.

8. Defendant Charles E. Johnson ("Johnson") is a party in his official capacity as the Acting Secretary of the United States Department of Health and Human Services, having offices at 200 Independence Avenue, S.W., Washington, D.C. Defendant Johnson has been delegated the authority by the Congress of the United States to administer the FDCA.

9. Defendant Frank M. Torti ("Torti") is a party in his official capacity as the Acting Commissioner of Food and Drugs, the head of and highest ranking official within FDA, which has offices at 5600 Fishers Lane, Rockville, Maryland and 200 C. Street, S.W., Washington D.C. Defendant Johnson, as Acting Secretary of Health and Human Services, has delegated to defendant Torti the authority to administer the drug approval provisions of the FDCA through FDA.

10. Defendant FDA is an agency within the Public Health Service, which is a part of Health and Human Services. The FDA has offices at 5600 Fishers Lane, Rockville, MD.

JURISDICTION AND VENUE

11. This case arises under the Administrative Procedure Act ("APA"), 5 U.S.C. § 551, et seq.; the FDCA, 21 U.S.C. § 301 et seq., as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (commonly referred to as the "Hatch-Waxman Act") (codified as amended in relevant part at 21 U.S.C. § 355 and 35 U.S.C. § 271); and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

12. By granting NCE exclusivity to Vyvanse and refusing to file and review Actavis' ANDA, FDA has issued a final agency action, which presents an actual controversy for which Actavis is entitled to review and relief under 5 U.S.C. § 701 et seq.

13. Actavis has standing to maintain this action pursuant to the APA, as a legal entity that has suffered a legal wrong and has been adversely affected by final agency action, as complained of herein.

14. There exists an actual, justiciable case or controversy between Actavis and FDA regarding FDA's grant of NCE exclusivity to Vyvanse and FDA's refusal to file and review Actavis' ANDA, as to which Actavis requires: (i) a declaration of rights by this Court; and (ii) injunctive relief against FDA.

15. This Court has jurisdiction over the subject matter of this action under, inter alia, 28 U.S.C. §§ 1331, 1361, 2201.

16. This Court has personal jurisdiction over defendants Johnson, Acting Secretary of Health and Human Services, and Torti, Acting Commissioner of Food and Drugs, in that the agency and the individual defendants conduct substantial business in the district.

17. Venue is proper in this judicial district by virtue of 28 U.S.C. § 1391.

FACTUAL BACKGROUND

New Drugs and Patent Listing Requirements

18. Before marketing a new drug in the United States, a manufacturer must submit an NDA to FDA, and FDA must approve it. Once approved, new drugs generally are referred to as brand name drugs because they are marketed under a trade name or trademark for the drug product rather than the chemical name for the active ingredient in the drug product.

19. Among other things, an NDA must contain technical data on the composition of the drug product, including its active ingredient, the means for its manufacture and a statement of its proposed uses. In addition, the manufacturer must submit evidence that the drug is safe and efficacious for its proposed uses.

20. FDA approves a new drug only if it determines that the drug is safe and efficacious for its proposed uses.

21. In addition to the technical data submitted in an NDA, a brand name drug manufacturer is required to submit to FDA information on each patent that claims the drug or a method of using the drug that is the subject of the NDA with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, sale or importation of the drug product. A brand name drug manufacturer should submit patent information – the patent's number and its expiration date – in connection with its NDA if the patent claims a drug or claims a method of using the drug covered by the NDA. 21 U.S.C. § 355(b)(1); 21 C.F.R. § 314.53.

22. Once FDA approves an NDA, FDA lists the patent information submitted by the brand name drug manufacturer in its publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" (commonly referred to as the "Orange Book"). 21 U.S.C. § 355(b)(1).

23. The Orange Book identifies drug products approved on the basis of safety and effectiveness by FDA under the FDCA. The Orange Book includes an index of drug products by trade or established name as well as drug patent and exclusivity information.

Generic Drugs and Patent Certification Requirements

24. A generic drug is a version of a brand name drug that is generally sold without a trade name or trademark for the drug product.

25. Before marketing a generic drug in the United States, a manufacturer must submit an ANDA to FDA, and FDA must approve it. An ANDA applicant must show that its generic drug is bioequivalent to the previously approved brand name drug.

26. Generic drugs typically enjoy a significant price advantage over their brand name counterparts. Consequently, generic drugs are frequently prescribed in an effort to control healthcare costs. Generic drugs represent an increasing portion of the medicines used in the United States.

27. The introduction of a generic drug as an alternative to a brand name drug typically results in a dramatic reduction in the brand name drug's market share. The high level of a generic drug's market penetration is due to its lower price, generic substitution requirements and preferred status in various reimbursement plans, among other things.

28. A generic drug manufacturer seeking FDA approval for a generic version of a brand name drug product listed in the Orange Book must file one of four certifications with FDA. 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.50(i). A certification that the patent claiming the brand name drug is invalid or will not be infringed by the manufacture, use or sale of the generic drug for which the ANDA is submitted is commonly referred to as a Paragraph IV certification.

29. In order to encourage the timely market entry of generic products, the Hatch-Waxman Act permits generic pharmaceutical companies to develop generic products and undertake other activities necessary to obtain FDA approval without being held liable for infringing the patent rights of others. 35 U.S.C. § 271(e)(1). The filing of an ANDA with a Paragraph IV certification, however, is deemed to be an act of

infringement, which can be grounds for a brand name drug manufacturer to commence an action for patent infringement against the ANDA applicant. See 35 U.S.C. § 271(e)(2).

New Chemical Entity Exclusivity

30. As part of the balance struck in the Hatch-Waxman Act between encouraging innovation and encouraging prompt generic competition, the Hatch-Waxman Act includes provisions that can extend the time a brand name drug manufacturer can market its drug without generic competition.

31. The Hatch-Waxman Act specifically provides that no ANDA may be filed with FDA for five years after an NDA is approved if the NDA contains "a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved" in any other NDA. 21 U.S.C. § 355(j)(5)(F)(ii). This is referred to as New Chemical Entity ("NCE") exclusivity.

32. According to Representative Waxman, NCE exclusivity was designed to "give the drug industry the incentives needed to develop new chemical entities whose therapeutic usefulness is discovered late when little or no patent life remains." See 130 Cong. Rec. H9113 (daily ed. Sept. 6, 1984). Congress wanted to assure that drug companies were rewarded for major innovations involving a new drug "by guaranteeing them a period of market exclusivity during which time they could recoup their developmental costs." See Exhibit B, Letter from Congressman Henry A. Waxman to Frank E. Young, Commissioner, Food and Drug Administration, August 5, 1985 at 1.

33. FDA promulgated regulations to implement the Hatch-Waxman Act. In doing so, FDA defined "new chemical entity" to mean "a drug that contains no active

moiety that has been approved by FDA in any other application submitted under section 505(b) of the act." 21 C.F.R. § 314.108(a).

34. "Active moiety" is defined by FDA to mean "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance." Id.

35. "Drug substance" is defined by FDA to mean "an active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body, but does not include intermediates use (*sic*) in the synthesis of such ingredient." 21 C.F.R. § 314.3(b).

36. FDA determined that covalent derivatives (other than esters) of an already approved active moiety are entitled to NCE exclusivity, but that non-covalent derivatives and esters of an already approved active moiety are not entitled to NCE exclusivity.

Shire's NDA No. 21-977 and NCE Exclusivity for Vyvanse

37. Shire is the holder of NDA No. 21-977. FDA approved NDA No. 21-977 on February 23, 2007. After receiving FDA approval, Shire began marketing the drug that is the subject of NDA No. 21-977 under the trade name Vyvanse.

38. The Orange Book identifies the active ingredient in Vyvanse as lisdexamfetamine dimesylate. Shire markets Vyvanse for use in the treatment of attention deficit hyperactivity disorder ("ADHD").

39. FDA granted Shire NCE exclusivity for Vyvanse, which is set to expire on February 23, 2012.

40. According to the Vyvanse product insert, "Lisdexamfetamine is a prodrug of dextroamphetamine. After oral administration, lisdexamfetamine is rapidly absorbed from the gastrointestinal tract and converted to dextroamphetamine, which is responsible for the drug's activity." (Exhibit A, Vyvanse Product Insert.)

41. The product insert goes on to state:

> Lisdexamfetamine is converted to dextroamphetamine and L-lysine, which is believed to occur by first-pass intestinal and/or hepatic metabolism. Lisdexamfetamine is not metabolized by cytochrome P450 enzymes . . . Plasma concentrations of unconverted lisdexamfetamine dimesylate are low and transient, generally becoming non-quantifiable by 8 hours after administration. (Id.)

42. FDA reviewers confirmed this assessment:

> In its intact form lisdexamfetamine dimesylate lacks stimulant properties and is pharmacologically inactive. When taken orally, the amide linkage is hydrolyzed in the gastrointestinal tract, releasing active d-amphetamine. Lisdexamfetamine is an amide conjugate comprised of L-lysine covalently bound to the amino group of d-amphetamine.

(Exhibit C, Clinical Review, Dec. 6, 2005 at 7.)

43. FDA's Division of Psychiatric Products agreed:

> All the available evidence indicates that [lisdexamfetamine] is inactive, including both in vitro assays and in vivo animal data. In vitro assays showed that lisdexamfetamine has no activity at DA, NE, and a variety of other receptors. In vivo assays suggest that all the activity of orally administered lisdexamfetamine is due to the d-amphetamine that is released from the prodrug.

(Exhibit D, Thomas P. Laughren, Director, Division of Psychiatric Products, February 21, 2007 Memo at 2.)

44. FDA's Division of Psychiatric Products went on to state that the data shows "that lisdexamfetamine does not bind at the DA and NE reuptake sites that underlie the sympathomimetic effects of amphetamines. Thus, on this basis,

lisdexamfetamine would not be expected to have any amphetamine-like activity." (Exhibit E, Thomas P. Laughren, Director, Division of Psychiatry Products, Feb. 23, 2007 Memo at 1.)

45. In addition to statements Shire made to FDA and FDA's own findings, statements in U.S. Patent No. 7,223,735 ("the '735 patent," Exhibit F), which is owned by Shire and listed in the Orange Book for Vyvanse, are consistent with these findings.

46. The '735 patent specification describes lisdexamfetamine as providing "a carrier and amphetamine which are bound to each other but otherwise unmodified in structure." (Exhibit F, '735 patent, col. 4, ll. 48-50.)

47. The '735 patent goes on to state that lisdexamfetamine "does not cross the blood brain barrier and is thus substantially absent from the central nervous system," (id. at col. 9, ll. 15-17), and that "the covalent modification may prevent stimulant activity by preventing the drug from crossing the blood-brain barrier." (Id. at col. 10, l. 66 – col. 11, l. 1.)

48. The claims of the '735 patent also describe the lisdexamfetamine as releasing "amphetamine as an active." (See, e.g., id., claims 1 and 18.)

49. Both Shire and its predecessor company, New River Pharmaceuticals, have also publicly stated in press releases that dextroamphetamine is responsible for Vyvanse's activity. (See, e.g., Exhibit G, Feb. 23, 2007 New River Press Release ("The combination [of dextroamphetamine covalently-linked to l-lysine] is rapidly absorbed from the gastrointestinal tract and converted to d-amphetamine, which is responsible for VYVANSE's activity."); Exhibit H, Oct. 25, 2007 Shire Press Release ("VYVANSE is a therapeutically inactive prodrug, in which d-amphetamine is covalently bonded to l-

lysine, and after oral ingestion it is converted to pharmacologically active d-amphetamine.").)

50. Lisdexamfetamine dimesylate is not pharmaceutically active, and lacks stimulant properties.

51. Lisdexamfetamine dimesylate is a covalent derivative of dextroamphetamine.

52. Upon oral ingestion, lisdexamfetamine is rapidly absorbed from the gastrointestinal tract and converted to dextroamphetamine. Dextroamphetamine is responsible for Vyvanse's therapeutic effect.

Actavis' ANDA Filing

53. On or about January 28, 2009, Actavis filed an ANDA, seeking approval to market generic lisdexamfetamine dimesylate capsules for use in the treatment of ADHD.

54. On or about January 28, 2009, by letter to Gary J. Buehler, Director of the Office of Generic Drugs, Center for Drug Evaluation Research, Food and Drug Administration, Actavis requested that FDA rescind the NCE exclusivity granted to Vyvanse and accept Actavis' ANDA for filing. Actavis' letter set forth the factual and legal basis for Actavis' position. On February 6, 2009, Actavis submitted to FDA a legal brief that further detailed its position.

55. On or about February 6, 2009, FDA informed Actavis that it was refusing to file Actavis' ANDA in light of FDA's award of NCE exclusivity to Vyvanse. (Exhibit I, Letter from CDER Electronic Document Staff to Janak Jadeja, February 6, 2009.) FDA also informed Actavis that it was returning the ANDA to Actavis. FDA recognized

that Actavis was challenging the NCE exclusivity associated with Vyvanse, but stated that it could not possess or review the ANDA while the NCE exclusivity was still in effect.

Vyvanse Is Not Entitled to NCE Exclusivity

56. In granting NCE exclusivity to Vyvanse, FDA applied a blanket rule that all covalent derivatives (other than esters) of previously approved drugs should be considered active moieties entitled to NCE exclusivity, while non-covalent derivatives should not.

57. FDA's distinction between covalent and non-covalent derivatives is arbitrary and capricious and contrary to law, including 21 U.S.C. § 355(j)(5)(F)(ii).

58. Specifically, 21 U.S.C. § 355(j)(5)(F)(ii) directs that NCE exclusivity be based on the approval of a new "active ingredient," which in the context of this provision means a new active moiety.

59. The active moiety, in turn, is the molecule or ion (or portion thereof) that provides the therapeutic effect at the site of drug action.

60. FDA's blanket distinction between covalent derivatives and non-covalent derivatives for purposes of awarding NCE exclusivity is inconsistent with the FDCA, its legislative history and FDA's own regulations.

61. Dextroamphetamine is the molecule that provides the therapeutic effect of Vyvanse at the site of drug action.

62. Dextroamphetamine is the active moiety in Vyvanse.

63. Vyvanse is not the first drug approved by FDA with dextroamphetamine as the active moiety providing the therapeutic effect at the site of drug action.

64. In 1976, FDA approved an NDA for Dexedrine. The active ingredient in Dexedrine is dextroamphetamine sulfate, which is a salt (a non-covalent derivative) of dextroamphetamine.

65. Other products previously approved by FDA where dextroamphetamine is an active ingredient include Adderall® and Biphetamine.

66. Because the active moiety in Vyvanse, dextroamphetamine, had already been approved in numerous previous applications, FDA's decision to grant NCE exclusivity to Vyvanse is arbitrary, capricious and contrary to law and, therefore, should be set aside.

Harm Suffered by Actavis

67. The improper grant of NCE exclusivity to Vyvanse and FDA's refusal to file and review Actavis' ANDA denies Actavis access to the market.

68. Every day that FDA refuses to file and review Actavis' ANDA delays final approval for Actavis' ANDA.

69. Without final FDA approval, Actavis cannot market its generic lisdexamfetamine product.

70. As a result of FDA's arbitrary, capricious and unlawful actions, Actavis is precluded from marketing the lisdexamfetamine product set forth in its ANDA and consumers are precluded from purchasing generic lisdexamfetamine.

CLAIM FOR RELIEF

71. Actavis repeats and realleges paragraphs 1-70 of the Complaint.

72. As set forth above, FDA's grant of NCE exclusivity to Vyvanse and its refusal to file and review Actavis' ANDA is arbitrary, capricious and contrary to the

plain meaning of the FDCA (21 U.S.C. § 355(j)(5)(F)(ii)), its legislative history and FDA's own regulations.

73. The active moiety in Vyvanse is dextroamphetamine, which has been approved in numerous applications prior to the approval of NDA No. 21-977. Therefore, FDA's decision to grant NCE exclusivity to Vyvanse is arbitrary, capricious and not in accordance with the law within the meaning of 5 U.S.C. § 706(2)(A), in excess of statutory authority within the meaning of 5 U.S.C. § 706(2)(C), and in violation of the FDCA.

74. FDA's refusal to file and review Actavis' ANDA due to FDA's grant of NCE exclusivity to Vyvanse constitutes final agency action that is reviewable by this Court.

75. FDA's refusal to accept and review Actavis' ANDA causes Actavis harm unless this Court issues injunctive relief setting aside Vyvanse's NCE exclusivity and compelling FDA to file and review Actavis' ANDA.

76. Actavis has exhausted its administrative remedies.

77. Actavis has no adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff Actavis Elizabeth LLC respectfully requests this Court to enter judgment in its favor against defendants Charles E. Johnson, Acting Secretary of Health and Human Services and Frank M. Torti, Acting Commissioner of Food and Drugs, United States Food and Drug Administration and the United States Food and Drug Administration as follows:

a. Entry of judgment declaring that FDA's grant of NCE exclusivity to Vyvanse is arbitrary, capricious and contrary to law;

b. Entry of judgment declaring that FDA's refusal to file Actavis' ANDA is arbitrary, capricious and contrary to law; and

c. Entry of an injunction directing FDA to rescind the NCE exclusivity for Vyvanse and directing FDA to accept the Actavis ANDA with an effective filing date of January 28, 2009 in order to place Actavis in the position it would have been in but for FDA's unlawful action; and

d. Such other and further relief as the Court deems just and proper.

Date: February 24, 2009

Respectfully submitted,

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