IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA	:	CRIMINAL NO. 08 -
v.	:	DATE FILED: 9-29-2008
CEPHALON, INC.	:	VIOLATION: 21 U.S.C. § 331(a), 333(a)(1) and 352(f)(1)
	:	(Distribution of misbranded drugs: inadequate directions for use - 1 count)
	:	Notice of forfeiture

INFORMATION

COUNT ONE

THE UNITED STATES ATTORNEY CHARGES THAT:

At all times material to this information:

1. Defendant CEPHALON, INC. ("CEPHALON") was a pharmaceutical corporation headquartered in West Chester, Pennsylvania. CEPHALON's primary business activity was the development, manufacture, promotion, and sale of prescription drugs.

2. The Federal Food, Drug and Cosmetic Act ("FDCA") governed the interstate distribution of drugs for human use. 21 U.S.C. § 301, et seq. In general, a drug manufacturer could not sell a drug in the United States until the Food and Drug Administration ("FDA") had approved the manufacturer's application, and determined that the drug was safe and effective, based on well controlled clinical studies, for the use proposed by the manufacturer. As part of its regulatory process, the FDA also reviewed the drug's "label" or "labeling," which had to include adequate directions for the intended use – that is, the use that the manufacturer proposed in seeking the FDA's approval.

3. The FDCA, at 21 U.S.C. § 352(f)(1), provided that a drug was misbranded if, among other things, the labeling did not contain "adequate directions for use." As the phrase was used in the FDCA, "adequate directions for use" could not be written for medical indications or uses for which the drug had not been proven to be safe and effective, through well-controlled clinical studies. Any uses for a drug that were not approved by FDA as safe and effective, and thus that were not included in the drug's approved labeling, were known as "off-label" indications or uses. A drug that was promoted for an off-label indication or use did not contain "adequate directions for use," because such an off-label indication or use was not included in the FDA-approved labeling for the drug, and that drug was therefore misbranded under Section 352(f).

4. From approximately January 2001 through at least 2006, defendant CEPHALON manufactured and sold Actiq, Gabitril, and Provigil, which were drugs within the meaning of the FDCA. 21 U.S.C. § 321(g)(1).

5. Defendant CEPHALON sold and shipped the drugs Actiq, Gabitril, and Provigil in interstate commerce, throughout the United States, accompanied by each drug's FDA-approved labeling, which bore adequate directions for each use of that drug that the FDA had approved.

Actiq

6. In 1998, the FDA approved Actiq for breakthrough cancer pain in opioid-tolerant patients.

7. From approximately January 2001 through at least 2006, defendant CEPHALON improperly promoted Actiq for non-cancer pain uses, such as injuries and

migraines. These additional intended uses were not approved by the FDA. In promoting Actiq for these new intended uses, CEPHALON caused the drug to be misbranded under 21 U.S.C. § 352(f)(1).

Gabitril

8. In 1997, the FDA approved Gabitril as an anti-epilepsy drug indicated as adjunctive therapy in adults and children 12 years and older in the treatment of partial seizures.

9. From approximately January 2001 through February 2005, defendant CEPHALON improperly promoted Gabitril to treat anxiety, insomnia, and pain. These additional intended uses were not approved by the FDA. In promoting Gabitril for these new intended uses, CEPHALON caused the drug to be misbranded under 21 U.S.C. § 352(f)(1).

Provigil

10. In 1998, the FDA approved Provigil to treat excessive daytime sleepiness associated with narcolepsy. In 2004, the FDA approved the expansion of Provigil's label to include the treatment of excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder.

11. From approximately January 2001 through at least 2006, defendant CEPHALON improperly promoted Provigil as a non-stimulant drug for the treatment of sleepiness, tiredness, decreased activity, lack of energy and fatigue. These additional intended uses were not approved by the FDA. In promoting Provigil for these new intended uses, CEPHALON caused the drug to be misbranded under 21 U.S.C. § 352(f)(1).

Cephalon's Off-label Promotional And Sales Practices

12. Defendant CEPHALON's management trained the sales force to disregard the restrictions of the FDA-approved label, and to promote CEPHALON's drugs for off-label uses.

13. Defendant CEPHALON's management directed its sales force to visit doctors who, due to the nature of their practices, normally would not prescribe CEPHALON's drugs to convince the doctors to prescribe the drugs for off-label uses. For example, the Actiq label stated that the drug was for "opioid tolerant cancer patients with breakthrough cancer pain, to be prescribed by oncologist or pain specialists familiar with opioids." Using the mantra "pain is pain," CEPHALON instructed the Actiq sales representatives to focus on physicians other than oncologists, including general practitioners, and to promote this drug for many uses other than breakthrough cancer pain. In the case of Gabitril, which had been approved for the treatment of partial seizures in epilepsy, CEPHALON told the sales force to visit not just neurologists (the specialty that normally treated epilepsy), but also psychiatrists, and to promote the drug for anxiety and other psychiatric indications.

14. Defendant CEPHALON trained its sales representatives on particular questioning techniques to use with their customer physicians to prompt off-label conversations about the company's drugs.

15. Defendant CEPHALON compensated its sales representatives through sales quotas and a bonus structure designed to encourage off-label promotion of its drugs. In effect, sales representatives generally could only reach their sales goals by promoting and selling off-label.

16. Because insurers, and third-party payors such as Medicaid, often do not reimburse for drugs when prescribed for off-label purposes, defendant CEPHALON instructed the sales representatives to coach the physicians on what diagnostic codes to record in their documentation. For example, CEPHALON instructed its sales representatives to advise doctors to use the diagnostic code for idiopathic hypersomnia when using Provigil to treat fatigue, an off-label indication, because Provigil would not be reimbursable if prescribed for fatigue.

17. Defendant CEPHALON employed sales representatives and retained medical professionals to speak to doctors about off-label uses of Actiq, Gabitril, and Provigil. The company funded continuing medical education programs, through millions of dollars in grants, to promote off-label uses of its drugs, in violation of the FDA's requirements. From 2001 to 2004, CEPHALON provided over $80 million for such grants.

18. As a way to increase off-label prescribing, defendant CEPHALON regularly sent doctors to lavish resorts for supposed "consultant" meetings to hear discussions about off-label uses of its drugs. The sales representatives invited those doctors believed to have the greatest potential for increasing their writing of CEPHALON prescriptions for off-label uses.

Risks to Patients

19. These off-label promotions, directed by defendant CEPHALON, caused patient harm, raised safety issues, and affected the proper treatment of patients. CEPHALON undertook these promotions for its own gain, despite the risk to patients' health and lives.

20. Actiq was an extremely powerful narcotic drug with a very narrow label. The FDA approved this drug for patients suffering breakthrough cancer pain, who had already developed a tolerance for opioid products (such as morphine); that is, the drug's label stated that

Actiq was approved for patients who suffered from such severe, persistent cancer pain that their opioid therapy was not effective. The approved label also required that the drug be prescribed by an oncologist or a pain specialist familiar with opioids. Actiq was a fentanyl product manufactured as a lollipop for the immediate delivery of pain relief. Because it was a strong and highly addictive narcotic, with significant potential for abuse, the FDA required defendant CEPHALON to submit quarterly reports about the company's efforts to manage the risks of the drug.

21. The use of Actiq could cause addiction, hypoventilation, or death, particularly in patients who were not already opioid-tolerant. Despite the restrictions in Actiq's label, and the known risks to patients, defendant CEPHALON promoted the drug for many types of pain, including migraines and sickle-cell pain crises, and in anticipation of changing wound dressings or radiation therapy. CEPHALON also promoted Actiq for use in patients who were not yet opioid tolerant.

22. The off-label use of Gabitril – approved for the treatment of epilepsy, but which defendant CEPHALON promoted for psychiatric uses – in fact caused seizures in certain patients who did not have epilepsy.

23. More generally, the promotion of an off-label use for a prescription drug can interfere with the proper treatment of a patient. Off-label promotion can lull a physician into believing that the drug being promoted is safe and effective for the intended off-label use, and that the FDA has approved the drug for that use. Thus, off-label promotion can cause a doctor and patient to forgo treatment with an FDA-approved drug that has been proven to be safe and

effective, and instead to substitute a treatment urged by the sales representative that is not known to be safe and effective, and that may in fact be harmful.

FDA's Warnings To Cephalon

24. In January 2002, shortly after defendant CEPHALON embarked on its off-label campaign promoting Provigil for wakefulness, the FDA sent CEPHALON a letter requiring the company to cease disseminating false and misleading written promotional materials representing that Provigil was better, safer, more effective, or useful in a broader range of conditions or patients than the FDA had approved. CEPHALON's written promotional materials included assertions that Provigil was useful for sleepiness, tiredness, decreased activity, lack of energy, and fatigue.

25. In February 2007, the FDA sent defendant CEPHALON a warning letter informing the company that a promotional piece that it distributed was

> false or misleading because it states or suggests that Provigil is safe and effective for use in the treatment of various disorders associated with fatigue, sleepiness, or inattentiveness, when in fact, Provigil is not indicated for fatigue at all and is indicated only for specific groups of patients with excessive sleepiness [as identified in the letter].

The FDA directed CEPHALON to cease immediately the dissemination of promotional materials for Provigil such as the material described in the FDA's letter.

26. In February 2005, once the FDA learned about seizures in some patients who had been prescribed Gabitril for conditions other than epilepsy, the agency issued a public health advisory. The FDA also required defendant CEPHALON to add a bolded warning on the Gabitril label advising doctors of the association between Gabitril and seizures in non-epileptic

patients, and to send a letter to doctors advising them of the Gabitril-seizure association. CEPHALON then stopped promoting this drug.

Profit to Cephalon

27. From approximately January 2001 through at least 2006, defendant CEPHALON profited financially by misbranding Actiq, Gabitril, and Provigil through off-label promotion, and distributing these drugs in interstate commerce.

28. From in or about January 2001 through in or about October 2001, in the Eastern District of Pennsylvania and elsewhere, defendant

CEPHALON, INC.

introduced into interstate commerce, and caused the introduction into interstate commerce, of quantities of Provigil, Gabitril, and Actiq, drugs within the meaning of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 321(p), which were misbranded under 21 U.S.C. § 352(f)(1), in that these drugs lacked adequate directions for their use, because CEPHALON promoted the drugs for uses that were outside of the drugs' labels, and that had not been approved by the Food and Drug Administration.

In violation of Title 21, United States Code, Sections 331(a), 333(a)(1), and 352(f)(1).

NOTICE OF FORFEITURE

THE UNITED STATES FURTHER CHARGES THAT:

1. As a result of the violations of Title 21, United States Code, Sections 331(a), 333(a)(1), and 352(f)(1) set forth in this information, defendant

CEPHALON, INC.

shall forfeit to the United States of America any quantities of Actiq, Gabitril, and Provigil, which between January 2001 and October 1, 2001 were misbranded when introduced into or while in interstate commerce, or while held for sale (whether or not the first sale) after shipment in interstate commerce, or which may not, under the provisions of Title 21, United States Code, Section 331, be introduced into interstate commerce.

2. If any of the property subject to forfeiture, as a result of any act or omission of the defendant:

(a) cannot be located upon the exercise of due diligence;

(b) has been transferred or sold to, or deposited with, a third party;

(c) has been placed beyond the jurisdiction of the Court;

(d) has been substantially diminished in value; or

(e) has been commingled with other property which cannot be divided without difficulty;

it is the intent of the United States, pursuant to Title 21, United States Code, Section 853(p), to seek forfeiture of any other property of the defendant up to the value of the property subject to forfeiture, that is $10,000,000.

All pursuant to Title 21, United States Code, Sections 334 and 853, and Title 28, United States Code, Section 2461(c).

LAURIE MAGID
ACTING UNITED STATES ATTORNEY