IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA	**:**	**CRIMINAL NO. _____**
v.	**:**	**DATE FILED: _____**
NOVARTIS PHARMACEUTICALS CORPORATION	**:**	**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**

I N F O R M A T I O N

COUNT ONE

THE UNITED STATES ATTORNEY CHARGES THAT:

At all times material to this information:

1. Defendant NOVARTIS PHARMACEUTICALS CORPORATION ("NPC") was a wholly-owned subsidiary of the global pharmaceutical company Novartis AG, a Swiss corporation headquartered in Basel, Switzerland. NPC was engaged in the development, manufacture, promotion, and sale of pharmaceutical drugs intended for human use. NPC distributed its pharmaceutical drugs throughout the United States.

2. Trileptal (also known by its chemical name, oxcarbazepine) was one of the drugs that NPC distributed. Trileptal was an anti-epileptic drug (known as an "AED").

3. The Federal Food, Drug, and Cosmetic Act ("FDCA"), among other things, governed the interstate distribution of drugs for human use, as codified in 21 U.S.C. § 301, et seq. The FDCA and its implementing regulations prohibited the distribution of any new drug in interstate commerce until the sponsor or manufacturer of that new drug had received approval

from the United States Food and Drug Administration (“FDA”), based on an intensive application and review process. 21 U.S.C. § 355.

4. The FDCA required that the sponsor of a new drug submit a New Drug Application ("application") to the FDA, which identified all of the proposed uses of the drug intended by that sponsor, together with the proposed labeling for those uses, and data, generated in randomized and well-controlled clinical trials, that demonstrated to the FDA's satisfaction that the drug would be safe and effective for those intended uses. 21 U.S.C. §§ 331(d) and 355(b).

5. Until the FDA found sufficient evidence of the drug's safety and efficacy for the uses proposed by the sponsor and approved the application, including the proposed labeling, the FDCA prohibited the sponsor from introducing the new drug into interstate commerce. 21 U.S.C. §355(a). Only after the FDA approved the application was the sponsor permitted by law to promote and market the drug, and then only for the medical conditions of use specified in the approved labeling. Uses not approved by the FDA, and not included in the drug's approved label, were known as "unapproved uses" or "off-label uses."

6. Under the FDCA, if the sponsor of a drug wanted to market that drug for an unapproved or off-label use, the sponsor first was required to submit to the FDA each additional proposed use, together with evidence, in the form of randomized and well-controlled clinical studies, sufficient to demonstrate that the drug was safe and effective for each additional proposed therapeutic use. The sponsor could not label or promote the drug for any new intended use without the prior approval of the FDA.

7. The FDCA provided that a drug was misbranded if, among other things, its labeling did not bear adequate directions for its use. 21 U.S.C. §352(f)(1). As the term was used

in the FDCA and its regulations, adequate directions for use could not be written for medical indications or uses for which the prescription drug had not been approved by the FDA. Prescription drugs that were promoted for uses that had not been approved by the FDA were thus deemed misbranded as a matter of law under Section 352(f)(l).

8. The FDCA prohibited the distribution in interstate commerce of a misbranded drug. 21 U.S.C. § 331(a) and (k).

FDA APPROVALS FOR TRILEPTAL

9. On or about January 14, 2000, the FDA approved NPC's application for the use of Trileptal as adjunctive therapy (used in addition to other drugs) or monotherapy (used alone) for the treatment of partial seizures in adults with epilepsy, and as adjunctive therapy for the treatment of partial seizures in children ages 4-16 with epilepsy.

10. Later in 2000, the FDA approved NPC's application for an expansion of Trileptal's label to include its use in children over 2 years old.

11. On or about August 7, 2003, the FDA approved NPC's application for an expansion of Trileptal's label to include its use as monotherapy in the treatment of partial seizures in children ages 4-16 with epilepsy.

NPC'S OFF-LABEL PROMOTION AND SALES PRACTICES

12. NPC launched Trileptal in or about January 2000, targeting specialists treating patients with epilepsy. Epilepsy was a brain disorder involving repeated, spontaneous seizures. A seizure was an episode of disturbed brain function, caused by abnormally excited electrical signals in the brain, that caused changes in attention or behavior. Epilepsy was normally treated

by neurologists and epileptologists (specialists), and by some primary care physicians (non-specialists).

13. NPC was disappointed with the first months' sales of Trileptal. The population of persons with epilepsy in the United States was fairly confined, and the number of persons with untreated epilepsy was relatively small. There were already several other anti-epileptic drugs on the market.

14. NPC identified significant market opportunities for Trileptal in the treatment of bipolar disorder (a psychiatric disease) and neuropathic (nerve) pain. The populations suffering from these diseases were far greater than those with epilepsy. The use of other AEDs to treat these diseases was growing, and some of the competitor AEDs had pending before the FDA applications for expanded labels for these uses.

15. The original application for Trileptal, submitted to the FDA in 1992, had sought an indication both for epilepsy and for mania, a term that forms part of the diagnosis of bipolar disease. (Patients suffering from bipolar disease cycle between some form of mania and some form of depression.) Clinical trials undertaken to test the efficacy of Trileptal for bipolar disease had failed to show positive results, and the application was withdrawn for approval for mania in or about August 1995.

16. Although defendant NPC knew that it lacked FDA approval and had only minimal scientific data to support the use of Trileptal in bipolar disorder or neuropathic pain, NPC decided to market and promote Trileptal as a treatment for both of these indications in or about July 2000 and directed its sales force to visit doctors who, due to the nature of their practices, normally would not prescribe Trileptal for its approved uses. For example, at this time

defendant NPC told the sales force to visit not just neurologists or epileptologists (the specialities that normally treat epilepsy), but also psychiatrists and pain specialists, who were known to use AEDs like Trileptal for off-label uses.

17. From approximately July 2000 through at least June 2004, defendant NPC unlawfully promoted Trileptal for the treatment of neuropathic pain and bipolar disorder. These intended uses were not approved by the FDA. In promoting Trileptal for these off-label uses, NPC caused the drug to be misbranded under 21 U.S.C. § 352(f)(1).

18. In re-launching Trileptal, defendant NPC's top management approved marketing and sales plans that identified the off-label opportunities in neuropathic pain and bipolar disease, and developed strategies to maximize sales in those areas. NPC trained, managed, and rewarded its sales staff for these off-label promotional efforts.

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

20. Defendant NPC retained medical professionals to speak to doctors about the off-label uses of Trileptal. The company funded continuing medical education programs to promote off-label uses of Trileptal.

21. In or about July 2001, defendant NPC submitted an application to the FDA to expand the label for Trileptal to include an indication for neuropathic pain. After clinical trials did not show Trileptal's efficacy in this use, NPC abandoned that application.

HARM CAUSED BY NPC'S OFF-LABEL PROMOTION

22. Defendant NPC's off-label promotion of Trileptal raised safety issues, affected the treatment of patients, and undermined the FDA drug approval process. NPC undertook this illegal off-label promotion for its own financial gain, despite the potential risk to patients' health and lives.

23. 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.

PROFIT TO NPC

24. Defendant NPC profited by hundreds of millions of dollars by misbranding Trileptal through off-label promotion, and distributing Trileptal in interstate commerce.

25. From in or about July 2000 through in or about December 2001, in the Eastern District of Pennsylvania and elsewhere, defendant

NOVARTIS PHARMACEUTICALS CORPORATION

introduced and caused the introduction into interstate commerce of quantities of Trileptal, a drug within the meaning of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321(g), which was intended for use in treating neuropathic pain and bipolar disorder, and which drug was

misbranded within the meaning of Title 21 United States Code, Section 352(f)(l), in that Trileptal's labeling lacked adequate directions for such uses.

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

NOTICE OF FORFEITURE

THE UNITED STATES ATTORNEY FURTHER CHARGES THAT:

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

NOVARTIS PHARMACEUTICALS CORPORATION

shall forfeit to the United States of America any quantities of Trileptal, which, between July 2000 and December 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 $15,000,000.

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

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ZANE DAVID MEMEGER
UNITED STATES ATTORNEY

EUGENE THIROLF
Director, Office of Consumer Litigation
United States Department of Justice