IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA, Plaintiff, v. AEGERION PHARMACEUTICALS, INC., a corporation, and DR. CHARLES M. GERRITS, an individual, Defendants.	No. _____

Plaintiff, the United States of America, by its undersigned counsel, respectfully represents to this Court as follows:

INTRODUCTION

1. The United States of America brings this action under the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 332(a), and the inherent equitable authority of this Court, to permanently enjoin and restrain Aegerion Pharmaceuticals, Inc. and Dr. Charles M. Gerrits (collectively, "Defendants"), from:

a. violating 21 U.S.C. § 331(a) by introducing or delivering, or causing to be introduced or delivered, into interstate commerce drugs that are misbranded within the meaning of 21 U.S.C. § 352(f)(1) and 352(y); and

b. violating 21 U.S.C. § 331(k) by misbranding or causing drugs to become misbranded within the meaning of 21 U.S.C. § 352(f)(1) and 352(y) while such drugs are held for sale after shipment of one or more of their components in interstate commerce.

JURISDICTION AND VENUE

2. This Court has jurisdiction over this matter under 21 U.S.C. § 332(a) and 28 U.S.C. §§ 1331, 1337, and 1345.

3. Venue in this District is proper pursuant to 28 U.S.C. § 1391(b) and (c).

DEFENDANTS

4. Defendant, Aegerion Pharmaceuticals, Inc. (Aegerion), is a Delaware corporation with its principal place of business in Cambridge, Massachusetts. Aegerion manufactures and distributes Juxtapid (generic name lomitapide), a drug that the United States Food and Drug Administration (FDA) approved on December 21, 2012 as an adjunct to other lipid-lowering therapies to treat adult patients with homozygous familial hypercholesterolemia (HoFH). Juxtapid is manufactured in Missouri using components from various states, including South Carolina. Aegerion distributes Juxtapid in its finished form throughout the United States. For example, Juxtapid is distributed to prescribers located in California, Florida, New York, New Jersey, Ohio, Pennsylvania, and Texas.

5. Defendant Dr. Charles M. Gerrits is Aegerion's Senior Vice President, Global Market Access, Patient Advocacy and REMS. He was hired by Aegerion and assumed this position in January 2017, after all the investigations described in the Complaint were completed, and had no responsibility for the violations observed. In this role, he is responsible for the management and oversight of the implementation, compliance, and maintenance of Aegerion's Risk Evaluation and Mitigation Strategy (REMS) programs, including the Juxtapid REMS Program, and related compliance activities. Therefore, Dr. Gerrits has the authority and duty to prevent, detect, and correct future violations of the FDCA.

RISKS ASSOCIATED WITH JUXTAPID

6. Juxtapid is approved as an adjunct to other lipid-lowering therapies to treat adult patients with HoFH, a rare form of the more common familial hypercholesterolemia (FH).

7. FH is a genetic disorder that prevents the removal of LDL-C, often called the "bad" cholesterol, from the blood, causing abnormally high levels of circulating LDL-C. Persons who inherit a defective LDL receptor gene (or a defective gene associated with the LDL receptor function) from one parent have heterozygous FH (HeFH). Persons who inherit defective LDL receptor genes from both parents have HoFH. Persons with HoFH develop dramatically early and severe atherosclerotic cardiovascular disease (CVD). Symptomatic CVD typically presents during the first two decades of life, often leading to heart attack, stroke, and death. If untreated, most HoFH patients do not survive past age 30 due to death from CVD.

8. The estimated prevalence of HeFH at the time of Juxtapid's approval was approximately 1 in 500 (roughly 638,000 persons in the United States based on a population of about 319 million), while the prevalence of HoFH was roughly 1-in-1 million (roughly 319 persons based on the current United States population).

9. Aegerion sought approval for Juxtapid for the treatment of HoFH under FDA's Orphan Drug Designation program, which encourages the development of medical products intended to treat rare diseases and conditions affecting fewer than 200,000 people in the United States. 21 U.S.C. § 360cc.

10. In December 2012, FDA approved Juxtapid as an adjunct to other lipid-lowering therapies to treat adult patients with HoFH. Juxtapid's label included information stating that the drug's safety and effectiveness had not been established in patients with hypercholesterolemia

who do not have HoFH and that the effect of Juxtapid on cardiovascular morbidity and mortality had not been determined.

11. A boxed warning on the FDA-approved label cautioned prescribers about the risk of hepatotoxicity (liver toxicity) when taking Juxtapid, including elevations in transaminases (enzymes indicative of liver damage) and hepatic steatosis (the accumulation of fat in the liver), which can lead to liver disease, including steatohepatitis and cirrhosis.

STATUTORY FRAMEWORK

12. In accordance with the FDCA, FDA is the agency of the United States responsible for protecting the health and safety of the public by assuring that, among other things, drugs intended for use in people are safe and effective for their intended uses and the labeling of the drugs are true and accurate. FDA regulates, among other things, the approval, manufacture, labeling, and shipment of drugs in interstate commerce.

13. A product is a drug within the meaning of the FDCA if it is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man," 21 U.S.C. § 321(g)(1)(B), or if it is "intended to affect the structure or any function of the body of man," 21 U.S.C. § 321(g)(1)(C).

14. Under the FDCA, Juxtapid is not only a drug, but also a "new" drug. A "new drug" is defined as any drug "the composition of which is such that the drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. § 321(p)(1).

15. A "new drug" may not be introduced or delivered for introduction into interstate commerce unless FDA has approved a new drug application (NDA) or an abbreviated new drug

application (ANDA) with respect to such drug, or such drug is exempt from approval under an investigational new drug application (IND). 21 U.S.C. § 355(a), (b), (i), and (j).

16. In 2006, Congress amended the FDCA and authorized FDA to require, either as part of initial drug approval or after a drug has been approved, that a drug manufacturer be subject to a risk evaluation and mitigation strategy (REMS) to ensure the benefits of the drug outweigh the risks pursuant to 21 U.S.C. § 355-1.

17. The FDCA provides that the REMS may include specific elements to ensure the benefits of the drug outweigh the risks, including, inter alia, a Communications Plan that provides for disseminating important risk information to healthcare providers pursuant to 21 U.S.C. § 355-1(e)(3).

18. Under the FDCA, a drug is misbranded if the responsible person, as defined by the statute, fails to comply with a REMS requirement. 21 U.S.C. § 352(y).

19. Under the FDCA, a drug is further misbranded if its labeling fails to bear "adequate directions for use." 21 U.S.C. § 352(f)(1). "Adequate directions for use" means directions under which a layperson could use a drug safely and for the purposes for which it was intended. 21 C.F.R. § 201.5. A prescription drug, by definition, cannot bear adequate directions for use by a layperson, but is exempt from the adequate-directions-for-use requirement if it, among other things, has FDA-approved labeling that provides adequate information for its safe and effective use by practitioners for all the purposes for which it is intended, including all purposes for which it is advertised or represented. 21 C.F.R. § 201.100(c)(1) & 201.100(d).

20. The FDCA prohibits the introduction or delivery, or the causing to be introduced or delivered into interstate commerce, drugs that are misbranded, 21 U.S.C. § 331(a), and

misbranding or causing drugs to become misbranded while such drugs are held for sale after shipment of one or more of their components in interstate commerce, 21 U.S.C. § 331(k).

FDA APPROVED JUXTAPID SUBJECT TO A RISK EVALUATION MITIGATION STRATEGY (REMS)

21. FDA determined that, as a condition of approval of Juxtapid, a REMS program is necessary to ensure that the benefits of the drug outweigh the risk of hepatotoxicity. The purpose of the Juxtapid REMS program was "to educate prescribers about the risks of hepatotoxicity associated with the use of Juxtapid and the need to monitor patients during treatment with Juxtapid as per product labeling" and "to restrict access to therapy with Juxtapid to patients with a clinical or laboratory diagnosis consistent with HoFH."

22. Juxtapid was only available through the Juxtapid REMS program if the following requirements were met:

a. Prescribers were trained on the risks associated with Juxtapid, appropriate patient selection and monitoring, and the REMS requirements, and upon completion of the training, prescribers enrolled in the REMS program;

b. Prescribers attested to the safe use of Juxtapid for each new prescription by completing a Prescription Authorization Form stating that Juxtapid was indicated as an adjunct treatment for HoFH and that the patient had "a clinical or laboratory diagnosis consistent with HoFH," among other attestations; and

c. Only specially certified pharmacies dispensed Juxtapid to patients.

23. Under the Juxtapid REMS, Aegerion is responsible for the implementation, maintenance, monitoring, and evaluation of the REMS Program to assure the drug's safe use, and is responsible for taking reasonable steps to improve implementation and compliance with the

Juxtapid REMS Program. As part of the Juxtapid REMS, Aegerion is required to submit an assessment at six months, and then annual REMS Assessments thereafter.

24. At market launch in January 2013, Juxtapid cost roughly $295,000 per patient per year. The annual cost of Juxtapid later increased to over $330,000 per patient per year.

FDCA VIOLATIONS

25. Among the elements to assure safe use of Juxtapid, required by FDA under 21 U.S.C. § 355-1(f)(3), is an attestation from a prescriber for each new prescription, including prescriptions to increase dosage, that a patient had a "laboratory or clinical diagnosis consistent with HoFH." Aegerion violated the FDCA, 21 U.S.C. § 352(y), by failing to comply with this REMS requirement as follows:

a. Aegerion sales representatives told doctors that it would be truthful to sign attestations that patients' diagnoses were consistent with HoFH if any isolated aspect of patients' diagnoses were consistent with the isolated characteristics of any genetically-diagnosed HoFH patient. For example, Aegerion routinely distributed Juxtapid based on a representation that a treated LDL level of 152 was consistent with a diagnosis of HoFH based on the existence of a single genetically-diagnosed HoFH patient in the Juxtapid study. Aegerion did not tell doctors that the study patient was very young, with multiple physical manifestations of HoFH as a child, on multiple maximum treatments of other cholesterol-lowering drugs, and on apheresis. At the same time, Aegerion encouraged doctors to prescribe Juxtapid for patients with treated LDL levels of 152 and lower and to patients as old as 80 years old, without providing doctors with material information regarding typical treated LDL levels in geriatric patients.

b. Aegerion sales representatives caused the completion of attestations for prescribers by using prescribers' signature stamps.

c. Aegerion sales representatives targeted nurse practitioners as Juxtapid prescribers and "REMS-trained" the nurse practitioners, but Aegerion sales representatives did not "REMS-train" the physicians who must sign off on nurse practitioners' clinical work, with the result that physicians approved prescriptions without REMS required training and without knowing about the required REMS diagnostic attestation in violation of the Juxtapid REMS.

d. In order to make non-HoFH patients appear to be HoFH patients on forms submitted to FDA for the Juxtapid REMS program, Aegerion sales representatives filled out statements of medical necessity for physicians using false and misleading information, including total cholesterol levels (high density lipoprotein plus LDL) in place of LDL cholesterol levels; untreated LDL levels in place of treated LDL levels; and false medical histories (including the existence of xanthomas and tried-and-failed medications). As a result, Aegerion failed to implement and monitor the REMS elements to assure safe use.

e. In late 2013, after Aegerion added a check-box for a diagnosis consistent with HoFH to the Juxtapid statement of medical necessity, Aegerion sales representatives checked the box for physicians while completing prescription documentation for the physicians.

f. Rather than following the REMS requirement to distribute Juxtapid only for the narrow indication for which it was approved, Aegerion instead sought to render

the diagnosis of HoFH as vague and indefinite as possible in order to capture the HeFH and statin-intolerant patient populations as markets for Juxtapid.

g. By failing to comply with this REMS requirement, Aegerion misbranded Juxtapid, under 21 U.S.C. § 352(y).

26. Another element of the Juxtapid REMS Program, consistent with 21 U.S.C. § 355-1(g)(2)-(3), are the Annual Assessment Reports. Aegerion violated the FDCA, 21 U.S.C. § 352(y), by failing to comply with this REMS requirement as follows:

a. In or around June 2013, Aegerion submitted a REMS Assessment Report to FDA.

b. In or around August 2013, FDA asked Aegerion to explain why the median age of the patients receiving Juxtapid was 57 years old when the median age of patients in the Juxtapid HoFH study was only 31.

c. In or around December 2013, Aegerion filed a second REMS Assessment Report in which it told the FDA that the age difference between the patients in the clinical study and those being prescribed Juxtapid post-approval could be attributed to the different standards of care used in academic centers, where most of the patients in the Juxtapid HoFH study had been treated, and the standards of care used in community cardiology practices, where Aegerion was finding its business. Aegerion did not disclose to the FDA that it was distributing Juxtapid using a definition of HoFH that was inconsistent with Aegerion's pre-approval filings with the FDA and did not correspond to any peer-reviewed clinical standard for diagnosing HoFH, and was thus inconsistent with the goals of the Juxtapid REMS program.

d. By filing a misleading REMS Assessment Report in December 2013, Aegerion failed to comply with 21 U.S.C. § 355-1(g)(3), a requirement of the REMS program, and thus caused Juxtapid to become misbranded under 21 U.S.C. § 352(y).

27. Aegerion further caused Juxtapid to become misbranded under 21 U.S.C. § 352(f)(1) because it failed to provide adequate directions for all of the uses for which it distributed Juxtapid, including for treating "hypercholesterolemia," "familial hypercholesterolemia," and for treating other diseases and populations that were inconsistent with Juxtapid's approved indication and also the goals of the Juxtapid REMS. Juxtapid did not qualify for any exemptions from the requirement that it bear adequate directions for all its intended uses. For example:

a. Aegerion trained its sales force that the United States market for hypercholesterolemia could be clinically segmented into ranges based on a patient's LDL cholesterol level while on optimal or maximum lipid-lowering therapies: "refractory HeFH" from 100 to 200; "severe refractory (SR) HeFH" from 200 to 300; "phenotypic HoFH" from 300 to 450; and "classic HoFH" over 400. In January 2013, senior Aegerion executives and sales managers trained the Aegerion sales force to abandon the documented clinical segmentation of refractory HeFH, severe refractory HeFH, phenotypic HoFH, and classic HoFH, which the sales force had been trained to include since December 2012; instead, senior Aegerion executives and sales managers trained the sales force to sell Juxtapid as a treatment for severe high cholesterol generally without respect to a diagnosis consistent with HoFH. Specifically, Aegerion executives and managers trained the sales force to market Juxtapid based on "The Art of Not Defining" HoFH and reinforced that

strategy on weekly conference calls and in further trainings. The purpose of "The Art of Not Defining" HoFH was to unlawfully increase the population of patients to whom Juxtapid was marketed, notwithstanding Jutaxpid's Orphan Drug status and its REMS. Aegerion accomplished this by: first, discouraging the use of genetic testing (notwithstanding information in Aegerion's possession that genetic testing was the best and most reliable method for diagnosis and that testing capacity and availability in the United States was more than sufficient to test suspected HoFH patients); and second, by discouraging the use of any established, published, peer-reviewed diagnostic criteria. Aegerion management instructed and expected the sales force to sell Juxtapid for the treatment of "severe refractory lipid" patients, including those with HoFH, severe refractory HeFH, statin intolerance, or other diseases, such as diabetes, associated with treatment-resistant high cholesterol.

b. Aegerion sales managers trained sales representatives to distribute Juxtapid without mentioning HoFH. Many sales representatives regularly told doctors that Juxtapid was approved for treatment of "FH" (i.e., both HoFH and HeFH regardless of severity) and that appropriate Juxtapid patients included any who had not reacted adequately to other lipid-lowering therapies, because, Aegerion claimed, poor response to therapy was "consistent" with HoFH.

c. Initially, Aegerion sought to market Juxtapid to lipidologists at elite academic centers; however, Aegerion soon found that academic lipidologists resisted Aegerion's efforts to "not define" HoFH so it would include a broader population of refractory high cholesterol patients.

d. Aegerion shifted its marketing focus to community cardiologists, who were often much less knowledgeable about HoFH than academic lipidologists. By focusing on community cardiologists, Aegerion sales representatives were able to execute Aegerion's commercial strategy of distributing Juxtapid for use in patients who could not be diagnosed with HoFH but who had certain isolated characteristics consistent with aspects of HoFH.

e. One senior Aegerion executive explained, "[I]f you ask most clini[cal] card[iologists] if they have patients with FH they will say that do not know and if you ask if they have HoFH [patients] they will say no. . . . [W]e start our calls and market research first asking if they have [patients] that are difficult to treat with [maximum tolerated treatment] and then lead them down the pathway that it could be HoFH [] showing the variability in [LDL] and other characteristics from our [Juxtapid] study."

f. With managerial approval and pursuant to management direction, Aegerion sales representatives "helped" doctors identify Juxtapid patients whose clinical profiles did not correspond to the peer-reviewed and established clinical diagnostic criteria for HoFH, at times with LDL levels approaching the national average for healthy Americans. For example, one sales representative helped a doctor identify patients for treatment with Juxtapid with treated LDL levels from 100 to 135. Another sales representative helped a provider identify numerous patients for treatment with Juxtapid with treated LDL levels just over 100.

g. Aegerion sales managers trained sales representatives to tell prescribers and patients that use of Juxtapid would "take patients out of harm's way" and prevent

"impending" heart attacks or strokes even though Aegerion possessed no data showing that use of Juxtapid had any meaningful effect on cardiovascular mortality or morbidity. For example, one sales representative told doctors and their patients that the patients would have strokes if they did not take Juxtapid. Such false and misleading statements deceived community cardiologists and patients into believing that Juxtapid by itself could save patients from death or injury, which was inconsistent with its approval as an adjunct to other lipid-lowering therapies to treat adult patients with HoFH.

h. Aegerion executives and sales managers also specifically trained sales representatives to distribute Juxtapid to treat statin-intolerant patients, and many sales representatives did so.

i. Aegerion executives, including the then-Chief Executive Officer and sales managers, also specifically encouraged, approved, and oversaw distribution of Juxtapid for use in pediatric patients.

j. Aegerion further promoted and distributed Juxtapid for use as a monotherapy, i.e., not as an adjunct therapy to other lipid-lowering therapies.

28. Based on the conduct of Aegerion's sales force, at the direction of Aegerion senior management, Aegerion caused numerous health care providers to prescribe Juxtapid to numerous HeFH, statin-intolerant and diabetic patients, including elderly and pediatric patients, even though Juxtapid's labeling does not include, nor is it exempt from including, adequate directions for use in such patients or for use in lowering cardiac risk or for use as a monotherapy.

29. Numerous HeFH, statin-intolerant, and diabetic patients, including elderly and pediatric patients, suffered adverse events, including liver toxicity and gastrointestinal distress, and had to discontinue use of Juxtapid.

30. Aegerion introduced or caused to be introduced into interstate commerce drugs that are misbranded within the meaning of 21 U.S.C. § 352(f)(1) and 352(y), in violation of 21 U.S.C. § 331(a).

31. Aegerion misbranded or caused drugs to become misbranded within the meaning of 21 U.S.C. § 352(f)(1) and 352(y) while such drugs were held for sale after shipment of one or more of their components in interstate commerce in violation of 21 U.S.C. § 331(k).

32. Accordingly, unless restrained by this Court, Defendants are likely to continue to violate the Act, 21 U.S.C. § 331(a) and 331(k).

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully requests that this Court:

I. Permanently restrain and enjoin, under 21 U.S.C. § 332(a), Defendants and each and all of their directors, officers, agents, representatives, employees, attorneys, successors, assigns, and any and all persons in active concert or participation with any of them (including individuals, directors, partnerships, corporations, subsidiaries, and affiliates), who receive notice of the Court's order from violating 21 U.S.C. § 331(a) by introducing or delivering, or causing to be introduced or delivered, into interstate commerce drugs that are misbranded within the meaning of 21 U.S.C. § 352(f)(1) and 352(y); and violating 21 U.S.C. § 331(k) by misbranding or causing drugs to become misbranded within the meaning of 21 U.S.C. § 352(f)(1) and 352(y) while such drugs are held for sale after shipment of one or more of their components in interstate commerce; and

II. Order Defendants and each and all of their directors, officers, agents,

representatives, employees, attorneys, successors, assigns, and any and all persons in active concert or participation with any of them (including individuals, directors, partnerships, corporations, subsidiaries, and affiliates), who receive notice of the Court's order to cease, directly or indirectly, receiving, processing, manufacturing, preparing, packaging, holding, and distributing any article of drug within the meaning of 21 U.S.C. § 321(g), at or from Defendants' facility (and any other or new location at or from which Defendants receive, process, manufacture, prepare, pack, hold, or distribute drugs), unless and until Defendants bring their operations into compliance with the FDCA and its implementing regulations to the satisfaction of FDA; and

III. Order that Plaintiff be granted judgment for its costs herein, and that this Court grant such other and further relief as it deems just and proper.

Dated this 21st day of September, 2017.

Respectfully submitted,

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