



TRANSMITTED BY FACSIMILE

Marc Beer
Chief Executive Officer
Aegerion Pharmaceuticals, Inc.
101 Main Street, Suite 1850
Cambridge, MA 02142

RE: NDA 203858
JUXTAPID™ (lomitapide) capsules, for oral use
MA #31

WARNING LETTER

Dear Mr. Beer:

This letter notifies Aegerion Pharmaceuticals, Inc. (Aegerion) that the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has become aware of statements that you made regarding JUXTAPID™ (lomitapide) capsules, for oral use (Juxtapid) during broadcast interviews on CNBC's television show, "Fast Money," that aired on June 5, 2013, and October 31, 2013. The statements provide evidence that Juxtapid is intended for new uses, for which it lacks approval and for which its labeling does not provide adequate directions for use, which renders Juxtapid misbranded within the meaning of the Federal Food Drug and Cosmetic Act (FD&C Act) and makes its distribution violative of the FD&C Act. See 21 U.S.C. 352(f)(1), 331(a); 21 CFR 201.5, 201.100, 201.115, 201.128.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Juxtapid.¹

According to the INDICATIONS AND USAGE section of the FDA-approved product labeling (PI) for Juxtapid (emphasis original):

JUXTAPID is indicated as an adjunct to a low-fat diet and other lipid lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

¹ This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional activities cited in this letter.

Limitations of Use

- The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do not have HoFH.
- The effect of JUXTAPID on cardiovascular morbidity and mortality has not been determined.

Juxtapid is associated with a number of serious risks. Specifically, the PI includes a Boxed Warning regarding the risk of hepatotoxicity. Due to this risk, Juxtapid is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS), where healthcare providers and pharmacies must be certified in order to prescribe and distribute Juxtapid. Juxtapid is contraindicated in patients who are pregnant, with the concomitant use of strong or moderate CYP3A4 inhibitors, and in patients with moderate or severe hepatic impairment or active liver disease. The PI also contains Warnings and Precautions regarding the risk of embryo-fetal toxicity, reduced absorption of fat-soluble vitamins and serum fatty acids, gastrointestinal adverse reactions, concomitant use of CYP3A4 inhibitors, risk of myopathy with concomitant use of simvastatin or lovastatin, risk of supratherapeutic or subtherapeutic anticoagulation with warfarin, and risk of malabsorption with rare hereditary disorders of galactose intolerance.

The most common adverse reactions associated with Juxtapid (incidence $\geq 28\%$) are diarrhea, nausea, vomiting, dyspepsia, and abdominal pain.

Lack of Adequate Directions for Use

On June 5, 2013, during an interview on CNBC's television show, "Fast Money," you made the following statements with regard to Juxtapid:

- "In these [HoFH] patients, they have a devastating disease. They have a lethal level of cholesterol, bad cholesterol, which we call LDL, going through their blood stream. And they're born with this disease and often not diagnosed until 8, 10 years of age when they have a heart attack. If you can imagine a child having a heart attack at 8, 10, 12 years of age. And then they have another event, usually about every 18 months, and die by the age of 30. And we've found out that we can lower it significantly with this drug. . . ."
- "It's a devastating disease that causes early death. And the drug is corrective against that disease and that's the most important thing. If you think about some oncology products that may lengthen life three months or six months, this product has the potential of taking a patient that would die at 30 and allow them to meet their grandkids."

On October 31, 2013, during another appearance on CNBC's television show, you made additional statements with regard to Juxtapid, including:

- "These patients are going to die of a cardiac event, either a stroke or a heart attack, if we don't have them on therapy."

These statements misleadingly suggest that Juxtapid is safe and effective for use in decreasing the occurrence of cardiovascular events including heart attacks and strokes, and increasing the lifespan of patients with HoFH, and thus will have an effect on cardiovascular morbidity and mortality as well as overall mortality. However, Juxtapid is approved only for use as an adjunct to a low-fat diet and other lipid lowering treatments, to reduce specific lipids (see indication above) in patients with HoFH; its PI specifically includes a limitation of use stating that the effect of the drug on cardiovascular morbidity and mortality has not been determined. Furthermore, the statements made regarding Juxtapid misleadingly suggest that Juxtapid is safe and effective as a monotherapy. Juxtapid's labeling limits its use to use as an adjunct to other therapies, and use as a monotherapy is an unapproved use. The approved labeling for Juxtapid does not provide instructions for, or otherwise indicate that Juxtapid will be safe and effective if used, either to reduce the occurrence of cardiovascular events in HoFH patients and to increase their lifespans, or as a stand-alone therapy for reducing lipids in these patients. Information sufficient to demonstrate that Juxtapid is safe and effective for any of these new intended uses has not been submitted to FDA in an application.

In sum, the statements cited above provide evidence that Juxtapid is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use.

Additionally, while the statements cited above include substantial and repeated efficacy claims for Juxtapid, the presentation fails to communicate **any** of the risks associated with these new intended uses or its approved use. As previously noted, Juxtapid's PI in fact includes a Boxed Warning regarding potential liver toxicity, and the product is subject to an associated REMS. The repeated statements regarding Juxtapid, including the claims that patients taking the drug will "meet their grandchildren," misleadingly suggest that Juxtapid lacks significant risks.

Conclusion and Requested Action

For the reasons discussed above, your statements provide evidence that Juxtapid is intended for new uses, for which it lacks approval and for which its labeling does not provide adequate directions for use, which renders Juxtapid misbranded within the meaning of the FD&C Act and makes its distribution violative of the FD&C Act. See 21 U.S.C. 352(f)(1), 331(a); 21 CFR 201.5, 201.100, 201.115, 201.128.

OPDP requests that Aegerion immediately cease misbranding Juxtapid and introducing it into interstate commerce for unapproved uses for which it lacks adequate directions. Please submit a written response to this letter on or before November 22, 2013, stating whether you intend to comply with this request, listing any promotional materials (with the 2253 submission date) for Juxtapid that contain statements such as those described above, and explaining your plan for discontinuing use of such materials or, in the alternative, your plan to cease distribution of Juxtapid. Because the violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to correct any misimpressions about the approved use of Juxtapid.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA #31 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Warning Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your distribution of Juxtapid complies with each applicable requirement of the FD&C Act and FDA implementing regulations.

Failure to correct the violations discussed above may result in FDA regulatory action without further notice, including, but not limited, to seizure or injunction.

Sincerely,

{See appended electronic signature page}

Robert Dean, MBA, RAC
Division Director
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT T DEAN
11/08/2013