

APPENDIX 4

DEAR PROFESSIONAL SOCIETY LETTER

Important Drug Warning

Subject: Risk of hepatotoxicity with JUXTAPID™ (lomitapide) capsules
Appropriate patient selection and monitoring
Prescriber Action: Training and enrollment as part of REMS Program

January 11, 2013

Dear Professional Association:

This letter highlights important safety information your members need to know when prescribing JUXTAPID. To ensure the safe and appropriate use of JUXTAPID, it is important that you share the information included in this letter with your members who may treat patients with homozygous familial hypercholesterolemia (HoFH).

JUXTAPID™ (lomitapide) capsules, a microsomal triglyceride transfer protein (MTP) inhibitor 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).

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) for JUXTAPID. The purpose of the REMS is to help ensure that the benefits of treatment with JUXTAPID outweigh the **risk of hepatotoxicity**.

JUXTAPID has a **Boxed Warning** in the prescribing information.

WARNING: RISK OF HEPATOTOXICITY

- JUXTAPID can cause elevations in transaminases. In the JUXTAPID clinical trial, 10 (34%) of the 29 patients treated with JUXTAPID had at least one elevation in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) $\geq 3x$ upper limit of normal (ULN). There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR), or alkaline phosphatase.
- JUXTAPID also increases hepatic fat, with or without concomitant increases in transaminases. The median absolute increase in hepatic fat was 6% after both 26 and 78 weeks of treatment, from 1% at baseline, measured by magnetic resonance spectroscopy. Hepatic steatosis associated with JUXTAPID treatment may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis.
- Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment and then ALT and AST regularly as recommended. During treatment, adjust the dose of JUXTAPID if the ALT or AST are $\geq 3x$ ULN. Discontinue JUXTAPID for clinically significant liver toxicity.
- Because of the risk of hepatotoxicity, JUXTAPID is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the JUXTAPID REMS PROGRAM.

Appropriate Patient Selection

- JUXTAPID is indicated for use in patients with HoFH.
- Patients must have a clinical or laboratory diagnosis consistent with HoFH.
- JUXTAPID has not been studied in pediatric patients less than 18 years.

Prescriber Action

In order to prescribe JUXTAPID, prescribers must review the Prescribing Information and Prescriber Training Module, and enroll in the JUXTAPID REMS program.

Certified Pharmacies

JUXTAPID is only dispensed through certified pharmacies.

More specific details about prescriber responsibilities, enrollment and educational materials for JUXTAPID REMS Program can be found at www.JUXTAPIDREMSProgram.com. For more information, you may also contact JUXTAPID REMS Program toll-free at 1-85-JUXTAPID (1-855-898-2743).

The information in this letter is not intended as a complete description of the benefits and risks associated with the use of JUXTAPID. Please see accompanying Prescribing Information and Medication Guide.

Please share the information on the JUXTAPID REMS Program and the materials referenced above with your membership in order to ensure the safe and appropriate use of JUXTAPID. Thank you for your consideration of this request.

Sincerely,

Dr. Mark Sumeray
Chief Medical Officer

Aegerion Pharmaceuticals, Inc.
