



Zydus Discovery DMCC
C/O Zydus Healthcare (USA), LLC [US Agent]
Attention: G. Srinivas, Head of Regulatory Affairs
73 Route 31 North
Pennington, NJ 08534

RE: [REDACTED] (b) (4)
Saroglitazar Tablets
MA 1

Dear G. Srinivas:

As part of its monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a Zydus Discovery DMCC (Zydus) video titled, *Saroglitazar (Lipaglyn) Mechanism of Action*, regarding Saroglitazar Tablets (Saroglitazar), available on the website YouTube.com.¹ This video suggests, in a promotional context, that Saroglitazar (also referred to by the proprietary name "Lipaglyn™"), an investigational new drug, is safe and effective for the purposes for which it is being investigated or otherwise promotes the drug. As a result, Saroglitazar is misbranded under section 502(f)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C) Act. Section 301(a) of the FD&C Act prohibits the distribution of a misbranded product into interstate commerce.

Background

Saroglitazar is an investigational new drug for which there is no marketing authorization in the United States. [REDACTED] (b) (4)

Misbranding of an Investigational Drug

Under section 502(f)(1) of the FD&C Act, a drug shall be deemed to be misbranded unless its labeling bears adequate directions for use. Under FDA regulations, adequate directions for use means directions under which the layman can use a drug safely and for the purposes for which it is intended. 21 CFR 201.5. Your video describes the use of Saroglitazar in treating

¹ Found at <https://www.youtube.com/watch?v=FCOLhulst3M> (last accessed: December 19, 2016). The Zydus Discovery logo appears in this video around the 4:30 minute mark, along with identifiers of affiliated companies, Zydus and Cadila Healthcare, Ltd. The video was posted to YouTube by a representative of the Zydus Group. This video also appears on the Lipaglyn™ branded website for Saroglitazar at <http://lipaglyn.com/downloads.html> (last accessed: December 19, 2016).

patients with diabetic dyslipidemia and hypertriglyceridemia with Type 2 diabetes specifically. These uses are ones for which a prescription would be needed because they require the supervision of a physician and, therefore, for which adequate directions for lay use cannot be written.

Although 21 CFR 201.115(b) provides an exemption from the adequate directions for use requirement in section 502(f)(1) of the FD&C Act if a new drug “complies with section 505(i) . . . and regulations thereunder,” your investigational drug fails to do so. Among the requirements for the exemption for investigational drugs, 21 CFR 312.7 provides that “A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.”

The video includes claims and presentations that promote Saroglitazar as safe and effective for the purposes for which it is being investigated or otherwise promote the drug, including the following (emphasis original):

- SUPER: “Novel. Superior. Dual Acting”²
- SUPER: “**Lipaglyn**™
World’s first dual PPAR-alpha/gamma agonist approved for treating diabetic dyslipidemia”
- VOICEOVER (VO): “Lipaglyn is a novel, first in class therapy that brings in dual lipid and glycemic control in one molecule. . .”
- VO: “Lipaglyn ushers in a new age in diabetic dyslipidemia management.”

VO: “With 4 hydrogen bonding interactions, Lipaglyn binds a million times more to PPAR-alpha than fenofibrate. Lipaglyn, which is an alpha-alkoxy propionic acid derivative, it is structurally different from the other glitazars and glitazones and scores on the safety parameters.” Presented in conjunction with images and names of approved and unapproved comparator “glitazar” and “glitazone” molecules on screen

- VO: “Unlike other molecules it does not cause weight gain, edema, cardiac, renal, liver, or muscle toxicity.”
SUPER: “No weight gain” “No pedal oedema” “Has a non-renal route of elimination”

² This claim also appeared on a large exhibit banner prominently displayed above a Lipaglyn™ branded booth for Saroglitazar in the main exhibit hall, alongside approved products, at the American Diabetes Association 76th Scientific Sessions meeting from June 10th to 14th, 2016.

- SUPER: “LIPAGLYN™ is indicated for the treatment of diabetic dyslipidemia and hypertriglyceridemia with Type 2 diabetes mellitus not controlled by statin therapy.”

These claims and presentations promote an investigational new drug by suggesting that Saroglitazar is safe and effective for the treatment of patients with diabetic dyslipidemia and hypertriglyceridemia with Type 2 diabetes. For example, the claims and presentations, which refer to Saroglitazar by the proprietary name, “Lipaglyn”, make conclusions that the drug is “indicated for the treatment of diabetic dyslipidemia and hypertriglyceridemia with Type 2 diabetes mellitus,” is “superior” to other molecules, and is not associated with many serious risks that are generally attributed to these other molecules with similar mechanisms of action, when Saroglitazar has not been proven to be safe and effective within the meaning of the FD&C Act and has not been approved as a drug under that authority for any use. Although we acknowledge that Saroglitazar is approved for use in another country, the claims and presentations, including the broad statements regarding the drug’s approval as the “world’s first,” furthermore are misleading, suggesting that the drug is approved throughout the world, including in the United States, when that is not the case. The video does not include any specific information regarding Saroglitazar’s approval status in the world or any information to indicate that Saroglitazar is an investigational new drug that has not been approved for commercial distribution in the United States.

Conclusion and Requested Action

For the reasons discussed above, Saroglitazar is misbranded under section 502(f)(1) of the FD&C Act and in violation of section 301(a) of the FD&C Act. From a public health perspective, these claims and presentations are concerning because they include representations in a promotional context regarding the safety and efficacy of an investigational new drug that has not been approved by the FDA.

OPDP requests that Zydus immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before January 6, 2017, stating whether you intend to comply and explaining your plan for discontinuing use of such violative materials.

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**. A courtesy copy can be sent by facsimile to (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 1 in addition to the (b) (4) 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 Untitled 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 promotional materials for Saroglitazar comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Ankur Kalola, PharmD, RAC
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

{See appended electronic signature page}

Melinda McLawhorn, PharmD, BCPS, RAC
Team Leader
Division of Advertising & Promotion Review 2
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/

ANKUR S KALOLA
12/21/2016

MELINDA W MCLAWHORN
12/21/2016