



Chiasma Inc.
Attn: Ruth E. Stevens, PhD., MBA
Executive Vice President and Chief Scientific Officer
Camargo Pharmaceutical Services, LLC [Authorized Agent for Chiasma Inc.]
9825 Kenwood Road, Suite 203
Cincinnati, OH 45242

RE: [REDACTED] (b) (4)
octreotide capsules
MA 10

Dear Dr. Stevens:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a video posted on the website *YouTube.com* titled; *Experts Discuss New Advances in Acromegaly* by Chiasma, Inc., for the investigational new drug octreotide capsules.¹ The video suggests, in a promotional context, that octreotide capsules (also referred to by the proprietary name Mycapssa™), an investigational new drug, is safe and effective for the purpose for which it is being investigated or otherwise promotes the drug. As explained further below, octreotide capsules 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

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

[REDACTED] Chiasma issued a press release on April 18, 2016, addressing the complete response letter. Chiasma's press release,² titled "Chiasma

¹ Found at <https://www.youtube.com/watch?v=TzmkztSo0u4> (last accessed: December 21, 2016). This video also appeared on the Chiasma website at <http://www.chiasmapharma.com/about-treatment>

² The Chiasma Press Release announcing the FDA's complete response letter for octreotide capsules is available at: <http://ir.chiasmapharma.com/phoenix.zhtml?c=254057&p=irol-newsArticle&ID=2157743>. Accessed December 21, 2016.

Provides Update Regarding FDA's Complete Response Letter for Mycapssa™ New Drug Application", stated that "Upon completion of its review, the FDA advised Chiasma that the Agency did not believe the company's application had provided substantial evidence of efficacy to warrant approval, and advised Chiasma that it would need to conduct another clinical trial in order to overcome this deficiency. The FDA expressed concerns regarding certain aspects of the company's single-arm, open-label Phase 3 clinical trial and strongly recommended that the company conduct a randomized, double-blind and controlled trial that enrolls patients from the United States and be of sufficiently long duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment."

Misbranding of an Investigational New 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 octreotide capsules in treating acromegaly. This use is one for which a prescription would be needed because it requires 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 presents claims that promote octreotide capsules as safe and effective for the purpose for which it is being investigated or otherwise promote the drug, including the following:

The video contains the following claims and presentations in the main audio segment:

- (1:43) Dr. Shlomo Melmed: "I think the most important result of the trial was that the drug is safe and safety is a paramount concern for any new drug being used and the physician using the new drug should be assured and be able to reassure his or her patients that in fact the drug is safe. Secondly that the drug is efficacious and the effectiveness of the drug was proven in the clinical trials in that about 62% of patients who were known to respond to octreotide were shown to achieve the primary endpoint which was a maintenance of normal IGF 1 levels. Oral octreotide is a capsule of octreotide, the same octreotide which you use in your injections and which

is available to be swallowed and absorbed in the gastrointestinal system and exert its effects on the body similarly to the injectable octreotide.”

- (2:51) Jill Sisco: “I think that what matters most to patients is a) that it will work for them or that if it doesn’t work for them they can go to a different therapy and there is no harm no foul by trying a new oral alternative.”
- (3:12) Dr. Shlomo Melmed: “Well actually your comment about no harm is very important because it turns out from the studies that have been published to date that the side effects of oral octreotide are really quite similar to those that patients experience on the injectable so there doesn’t seem to be any unique side effect or downside to taking the oral as compared to the injectable so your comment about no harm is really quite important to patients. It’s a very exciting opportunity to be able to witness a development of a drug which is going to change the lives of so many patients with acromegaly.”

These claims make numerous positive and conclusory statements about the safety and effectiveness of octreotide capsules, such as suggesting that “the drug is safe” and “the effectiveness of the drug was proven in the clinical trials.” Thus, these claims suggest in a promotional context that octreotide capsules, an investigational new drug, is safe or effective for such uses, when FDA has not approved octreotide capsules for any use.

We acknowledge that the statement “Product is an investigational new drug and not available for commercial distribution,” is included as a SUPER on the screen for eight seconds at the end of the video. However, there is no disclaimer that would sufficiently mitigate the extensive claims and presentations throughout the majority of this video that suggest in a promotional context that octreotide capsules, an investigational new drug, is safe or effective for such uses, when FDA has not approved octreotide capsules for any use.

Conclusion and Requested Action

For the reasons discussed above, octreotide capsules 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 Chiasma 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 Amundson Avenue, 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 10 in addition to the [REDACTED] (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 octreotide capsules comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Charuni Shah, PharmD
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

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/s/

CHARUNI P SHAH
12/21/2016

MELINDA W MCLAWHORN
12/21/2016