Medisca Inc 11/25/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
New York District
158-15 Liberty Avenue
Jamaica, NY
11433

November 25, 2015

WARNING LETTER NYK-2016-12

VIA UNITED PARCEL SERVICE
DELIVERY SIGNATURE REQUESTED

Mr. Antonio Dos Santos, President
Medisca Pharmaceutique, Inc.
6090 Henri-Bourassa West
Saint-Laurent, Quebec
H4R3A6 Canada

Mr. Yigang Song, Quality Systems Manager
Medisca, Inc.
661 State Route 3
Plattsburgh, NY 12901

Dear Mr. Dos Santos and Mr. Song:

From February 17 to 27, 2014, a U.S. Food and Drug Administration (FDA) investigator conducted an inspection of your facility, Medisca, Inc., located at 661 Route #3, Unit C, Plattsburgh, NY 12901. FDA initiated this inspection after receiving reports of serious adverse events in patients who were administered drug products compounded using your active pharmaceutical ingredient (API) labeled as L-Citrulline. During this inspection, investigators collected six samples of APIs labeled as L-Citrulline that you repackaged for distribution to pharmacies for use in compounding. Subsequent FDA laboratory analysis of these samples determined that two of the samples were N-Acetyl-Leucine, a different amino acid. A Form FDA 483 was issued to your firm on February 27, 2014. FDA acknowledges Medisca's

March 7, 2014, response to the Form FDA 483. FDA also acknowledges Medisca's recall of eight lots of the L-Citrulline product after Medisca's own testing indicated that they did not contain L-Citrulline. The use of subpotent L-Citrulline and product incorrectly labeled as L-Citrulline in patients with certain urea cycle defects can lead to high ammonia levels, which is serious and potentially life-threatening.

Based on this inspection and sample analysis, it appears that your firm has produced drugs that violate the Federal Food, Drug, and Cosmetic Act (FDCA).

Adulterated Drugs

A portion of your APIs labeled as L-Citrulline are adulterated within the meaning of section 501(c) of the FDCA [21 U.S.C. § 351(c)], in that the drugs' strength differs from, and their purity and quality fall below that which the label purports or represented them to possess. As indicated above, samples from lots of repackaged APIs labeled as L-Citrulline were analyzed by FDA, and the analysis revealed that two of the samples were N-Acetyl-Leucine, a different amino acid than L-Citrulline.

Misbranded Drugs

Additionally, under section 502(a) of the FDCA [21 U.S.C. § 352(a)], a drug is misbranded if its labeling is false or misleading in any particular. The labeling of the lots of APIs that FDA analyzed and determined to be N-Acetyl Leucine is false and misleading because it stated that the API that was sampled was L-Citrulline. Therefore, these APIs are misbranded drugs in violation of section 502(a) of the FDCA.

Under section 301(a) of the FDCA [21 U.S.C. § 331(a)], the introduction or delivery for introduction into interstate commerce of any drug that is adulterated or misbranded is a prohibited act. Further, it is a prohibited act under section 301(k) of the FDCA [21 U.S.C. § 331(k)] to do any act with respect to a drug, if such act is done while the drug is held for sale after shipment in interstate commerce and results in the drug being adulterated or misbranded.

Corrective Actions

In your March 7, 2014 response to the Form FDA 483 you state that you have not categorized L-Citrulline as an API. FDA disagrees with this categorization. Your firm repackaged, relabeled and distributed L-Citrulline to compounding pharmacies and hospitals that, you were informed, used this product as a bulk drug substance in compounding drugs for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or animals. Furthermore, your APIs labeled as L-Citrulline contain the statements in 21 CFR 201.120(b) for drugs prepared, packaged, and primarily sold for use by pharmacists in compounding prescriptions. Additionally, the labeling, as well as advertising on your website, demonstrates your objective intent (as defined in 21 CFR 201.128) that the L-Citrulline API you introduce into interstate commerce is to be used as a bulk drug substance for pharmacy compounding.

Please provide details concerning your investigation regarding the extent of the product mix-up and any assurance you have that other APIs that you distributed, or will distribute, are not impacted.

Domperidone

FDA also received information indicating that your firm may be repackaging and distributing domperidone API to pharmacies for use in compounding drugs. Section 503A of the FDCA describes conditions that must be satisfied for compounded drug products to be exempt from certain sections of the FDCA: compliance with current good manufacturing practices (CGMP) (section 501(a)(2)(B)); labeling with adequate directions for use (section 502(f)(1)); and FDA approval prior to marketing (section 505). The exemptions provided in subsection 503A are not available to compounded drug products containing domperidone because domperidone is not the subject of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, is not a component of an FDA-approved drug under section 503A(b)(1)(A)(i) of the FDCA, and it does not appear on a list developed by the secretary under section 503A(b)(1)(A)(i)(III) of the FDCA.

Because drug products containing domperidone are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners, adequate directions cannot be written for them so that a layman can use these products safely for their intended uses. Consequently, their labeling fails to bear adequate directions for their intended uses, and would be misbranded. As stated above, section 301(a) of the FDCA prohibits the introduction or delivery for introduction into interstate commerce of any misbranded drug, and section 301(k) of the FDCA prohibits any act with respect to a drug if the act is done while the drug is held for sale after shipment in interstate commerce and results in the drug being misbranded. If you are repackaging and distributing the API domperidone you should stop immediately.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence and the occurrence of other violations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct and prevent the recurrence of violations, and provide copies of supporting documentation. If you cannot complete corrective actions within fifteen working days, state the reason for the delay and the timeframe within which you will have completed the corrections. Additionally, if you no longer manufacture or distribute L-Citrulline and do not manufacture or distribute domperidone, provide the dates and reasons you ceased manufacture or distribution. If you do not believe that the products discussed above are in violation of

the FDCA, include your reasoning and any supporting information for our consideration. Please identify your response with FEI # 1000120311.

Please send your reply to:

LCDR Catherine M. Beer, Compliance Officer
Food and Drug Administration
New York District
1 Winners Circle, Suite 110
Albany, NY 12205

Sincerely,
/S/
Ronald M. Pace
District Director
New York District