Vertical Pharmaceuticals, Inc 5/10/17

U.S. FOOD & DRUG ADMINISTRATION

New Jersey District Office
10 Waterview Blvd. 3rd Floor
Parsippany, New Jersey 07054

WARNING LETTER

May 10, 2017

VIA UNITED PARCEL SERVICE
RETURN RECEIPT REQUESTED

17-NWJ-04

Brian Markinson, Chief Executive Officer
Vertical Pharmaceuticals, Inc.
400 Crossing Boulevard
Bridgewater, New Jersey 08807

Dear Mr. Markinson:

This Warning Letter informs you of objectionable conditions observed during the U.S. Food and Drug Administration (FDA) inspection conducted at your firm, Vertical Pharmaceuticals, Inc. (Vertical), between October 24 and November 1, 2016. The inspection revealed serious violations of the Postmarketing Adverse Drug Experience (PADE) reporting requirements found in section 505(k) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 355(k)) and Title 21 of the Code of Federal Regulations (21 CFR 314.80). Failure to comply with section 505(k) is prohibited under section 301(e) of the Act (21 U.S.C. 331(e)).

At the conclusion of the inspection, an FDA investigator presented and discussed with you Form FDA 483, Inspectional Observations. We acknowledge receipt of a written response dated November 15, 2016, to the Form FDA 483 from Osmotica Pharmaceuticals LLC (Osmotica), an affiliate of Vertical.

From our review of the FDA Establishment Inspection Report, the documents submitted with that report, and Osmotica's written response dated November 15, 2016, we conclude that your firm did not adhere to the applicable

statutory requirements and FDA regulations for PADE reporting. Specific violations include, but are not limited to, the following:

1. Failure to develop written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences (ADEs) as required by 21 CFR 314.80(b).

As an application holder, your firm is required to develop written procedures for the surveillance, receipt, evaluation, and reporting of ADEs from any source to FDA. Our inspection determined that your firm does not have adequate written procedures that describe how you and your pharmacovigilance vendor acting on your behalf comply with PADE regulations.

Specifically, your firm does not have adequate written proceduresdescribing how incoming ADEs will be evaluated for seriousness and expectedness according to the current U.S. prescribing information. At the time of inspection, your written procedures required evaluation of adverse events by a service provider who was no longer in business, and referenced the use of MedWatch forms, which are obsolete. The standard operating procedure (SOP) in use at the time of inspection failed to assign the responsibility for investigation of serious and unexpected adverse drug experiences. There was no procedure for evaluating product complaints for adverse drug experiences, and no procedure for the exchange and evaluation of safety information with business partners. As a result of these deficiencies, your firm failed to evaluate and submit any 15-day Alert reports to the Divigel NDA-022038 since March 2014, when you acquired the NDA. During the inspection, we identified several ADE reports involving Divigel that your firm received but did not evaluate for seriousness and expectedness. The following three reports were determined to be 15-day Alert reports that were at least 50 days late and were not submitted to FDA until your firm's inspection:

- 2014-D005 (913 days late)
- 2015-D013 (672 days late)
- 2016-D011 (50 days late)

In your response, you prmided SOP RA-ooo8, "Receivingand Processing Adverse Events and Complaints," and stated that Osmotica's pharmacovigilance provider will be responsible for receiving ADE information from the call center, establishing reporting category, and preparing 15-day Alert Reports. However, we are unable to undertake an informed evaluation of your written response because you did not provide a corrective action plan that, if properly carried out, would prevent this type of violation in the future. Your response is unclear about how you intend to assess adverse drug experiences for reportability, and about who makes the final determinations of seriousness and expectedness. Furthermore, the revised procedures do not provide a mechanism to ensure the timely evaluation of adverse drug experience data received as a result of your business partner relationships. You also failed to determine whether Vertical is in possession of additional individual case safety reports that have not been evaluated for seriousness and expectedness and reported to FDA. These deficiencies raise serious concerns about your ability to monitor the safety profile of your products.

2. Failure to submit periodic adverse drug experience reports annually for an application which was approved three or more years ago as required by 21 CFR314.80(c)(2).

As an application holder of an approved new drug application (NDA-022038), you are required to submit Periodic Adverse Drug Experience Reports (PADERs). PADERs are required to include all individual case safety reports (ICSRs) not reported as 15-day Alert reports. Our inspection revealed that you failed to submit three annual PADERs to FDA since March 2014, when you acquired NDA-022038. You also failed to submit at least 25 non-15-day Alert reports to FDA since you acquired this NDA.

In your response, you provided SOPs RA-ooo8 and 006-14-AB, "Postmarketing Adverse Event Management. "However, we are unable to undertake an informed evaluation of your written response because you did not provide a corrective action plan that, if properly carried out, would prevent this type of violation in the future. Although Osmotica submitted the missing PADERs for NDA-022038, the SOPs provided in your response failed to include a procedure to ensure that all PADERs are complete and are submitted to the Agency in a timely manner.

Given the deficiencies above, we are concerned that your firm does not have a well controlled process for the surveillance, receipt, evaluation, and reporting of postmarketing ADEs to FDA. These deficiencies also raise concerns about your fundamental understanding of the PADE regulations and your firm's ability to monitor the safety of your drug products.

If you are considering an action that is likely to lead to a disruption in the supply of drugs produced at your facility, FDA requests that you contact CDER's Drug Shortages Staff immediately at **drugshortages@fda.hhs.gov, (mailto:drugshortages@fda.hhs.gov)**so that FDA can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you may have to report discontinuances or interruptions in your drug manufacturing under 21 U.S.C. 356C(b), and allows FDA to consider as soon as possible what actions, if any, may be needed to avoid shortages and to protect the health of the patients who depend on your products.

The violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your firm. It is your responsibility to ensure compliance with all requirements of federal law and FDA regulations. You should take prompt action to correct the violations cited in this letter. Failure to correct these violations promptly may result in legal action, including injunction, without further notice. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when awarding contracts. FDA may re-inspect your firm to verify that corrective actions have been completed.

Within 15 working days of your receipt of this letter, please notify this office in writing of the specific steps you have taken to correct the violations. Include an explanation of each step taken to prevent the recurrence of similar violations, as well as copies of any supporting documentation. If you cannot complete the corrective actions within 15 working days, state the reason for the delay and the time within which you will complete the correction. You may wish to include the dates by which each corrective action will be fully implemented.

If you have any questions, please contact Charles J.Chacko, Compliance Officer, New Jersey District. Address your written response and any pertinent documentation to U.S. Food and Drug Administration, 10 Waterview Boulevard., Parsippany, New Jersey 07054.

Sincerely,
/S/
Craig W. Swanson
Acting District Director
New Jersey District

More in 2017 (/ICECI/EnforcementActions/WarningLetters/2017/default.htm)