WARNING LETTER

8046255 Canada Inc. DBA Viatrexx

MARCS-CMS 596178 — JUNE 11, 2020

Delivery Method:

VIA UPS

Product:

Drugs

Recipient:

Mr. Stephen Emond

Chief Executive Officer

8046255 Canada Inc. DBA Viatrexx

1360 Rue Louis-Marchand
Beloeil QC J3G 6S3
Canada

Issuing Office:

Center for Drug Evaluation and Research | CDER

United States

Warning Letter 320-20-38

June 11, 2020

Dear Mr. Emond:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, 8046255 Canada Inc., doing business as (dba) Viatrexx, FEI 3010033797, at 1360 Rue Louis-Marchand, Beloeil, from September 16 to 24, 2019.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

In addition, FDA reviewed your labeling obtained from the inspection. Based on our review, your injectable homeopathic products “Articula,” “Mesenchyme,” “Connectissue,” “MuSkel-Neural,” “Ouch,” “Ithurts,” “Adipose,” “Systemic Detox,” “Hair,” “Neuro 3,” “Infla,” “Collagen,” “Prolo,” “Lymph 1,” “GI,” “Neuro,” “Arthros,” “Male+,” “Immunexx,” “Relief+,” “Intra-Cell,” “Facial,” and “ANS/CNS” (“injectable homeopathic

products") are unapproved new drugs under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 355. Introducing or delivering these products for introduction into interstate commerce violates section 301 of the FD&C Act, 21 U.S.C. 331.

These products are especially concerning from a public health perspective because injectable drug products can pose risks of serious harm to users; these risks are less likely to occur with topical or ingested products, i.e., those applied to the skin or taken by mouth. Injectable products are delivered directly into the body, sometimes directly into the bloodstream, and therefore, bypass some of the body's key defenses against toxins and microorganisms that can lead to serious and life-threatening conditions. Your injectable products are further concerning because they are labeled to contain potentially toxic or otherwise harmful ingredients, such as "Nux Vomica" (contains strychnine), "Rectum," and "Belladonna," thereby presenting additional risk of serious harm to patients when delivered directly into the body. Your firm's significant violations of current good manufacturing practice regulations, as described below, enhances the risk of harm to patients even further.

We reviewed your October 16, 2019, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigator observed specific violations including, but not limited to, the following.

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

You manufactured and distributed sterile injectable homeopathic drug products without adequately validating your aseptic manufacturing processes.

Process Simulations (Media Fills)

You failed to establish appropriate procedures and perform media fills to evaluate your manual aseptic filling and stoppering operations.

Filter Suitability

You failed to qualify the use of an appropriate filter for sterile filtration of your injectable drug products. Rather than using a sterilizing filter suitable for sterile drug manufacturing you used a **(b)(4)** filter for the sterile filtration. You also failed to test the filter integrity after use.

Poor Aseptic Techniques

You failed to ensure use of appropriate aseptic technique for manufacturing sterile injectable drug products. Our investigator observed personnel behaviors in the manual filling and stoppering operations that blocked the path of **(b)(4)** airflow.

On October 14, 2019, your firm recalled all sterile injectable drug products you manufactured. However, your proposed corrective actions permitted continued use of an unsuitable filter to sterilize your drug product. Your response also failed to address the frequency for conducting media fills.

Validation of aseptic processing requires establishing documented evidence with a high degree of assurance that a particular process consistently produces a product meeting its predetermined specifications and quality attributes. Media fills, and various systemic controls including, but not limited to, daily adherence to strict aseptic processing standards, suitable facilities, robust environmental control, and satisfactory product sterility testing, combine to ensure that an injectable drug is sterile. If injectable drugs are not sterile, they pose unacceptable risks to patients, including infection.

In response to this letter, provide the following:

• Comprehensive risk assessment of all contamination hazards with respect to your aseptic processes, equipment, and facilities, including an independent assessment that includes, but is not limited to:

o All human interactions within the ISO 5 area
o Equipment placement and ergonomics
o Air quality in the ISO 5 area and surrounding room
o Facility layout
o Personnel flows and material flows (throughout all rooms used to conduct and support sterile operations)

• A detailed remediation plan with timelines to address the findings of the independent contamination hazards risk assessment. Describe specific tangible improvements to be made to aseptic processing operation design and control.

• Your plan to ensure appropriate aseptic practices and cleanroom behavior during production. Include steps to ensure routine and effective supervisory oversight for all production batches. Also describe the frequency of quality unit oversight (e.g., audit) during aseptic processing and its support operations.

• Your plan to ensure robust sterilization processes for all sterilization methods. Provide your program for qualification and validation of all sterilization operations. Also, regarding sterilizing filtration, provide a corrective action and preventive action (CAPA) plan that ensures:

o Selection of a suitable **(b)(4)** filter for drug sterilization
o Appropriate filtration efficacy validation study protocols for each product and that incorporates the worst-case filtration conditions
o Proper responsibilities for proper conduct, full documentation, review, and approval of these studies
o Products will not be distributed before complete and adequate studies are performed

2. Your firm failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).

You failed to have appropriate gowning for manufacturing sterile injectable homeopathic drug products. With the exception of gloves, you used non-sterile gowning and also re-used these gowning materials to perform aseptic operations. Our investigator also observed exposed facial skin and the operator donning sterile gloves over bare hands when right next to the ISO 5 hood where aseptic processing is performed.

Your response stated that you will use sterile gowning for production. However, the gowning pictured in your response is not adequate for sterile injectable drug manufacturing because, for example, skin is exposed on the operator's face.

In response to this letter, provide the following:

• A list of the gowning materials you intend to use (e.g. sterilized nonshedding gowns and covers for the skin and hair, such as, face-masks, hoods, beard/moustache covers, protective goggles, and gloves).

• A gowning qualification program that establishes, both initially and on a periodic basis, the capability of an individual to adequately don the complete sterile gown in an aseptic manner.

• The role of the quality unit in gown supplier selection and ongoing qualification decisions. Ensure that the quality unit makes final decisions including supplier selection, release of raw materials and supplies (e.g., garments) used in production, and other ongoing decisions about supplier reliability.

• Details regarding how you will establish adequate gowning, training, gowning qualification, and supervision on an ongoing basis.

3. Your firm failed to establish a system for monitoring environmental conditions in aseptic processing areas and an adequate system for cleaning and disinfecting the room and equipment to produce aseptic conditions (21 CFR 211.42(c)(10)(iv) and (v)).

Cleaning and Disinfecting

Your procedures for cleaning and disinfecting are inadequate. For example, you lacked procedures to ensure frequent use of a **(b)(4)** agent. You also failed to consistently document cleaning and disinfecting.

Environmental Conditions

You performed environmental monitoring during the initial qualification of your facility in May 2019. However, you continued production through September 2019 with no routine environmental monitoring. You also lacked written procedures for environmental monitoring.

An environmental monitoring program provides meaningful information about the quality of the aseptic processing environment, as well as additional clean areas.

Your response is inadequate because it did not provide sufficient details or procedures for your environmental monitoring program. You also did not provide any evidence that your manufacturing environment is under an ongoing state of control.

In response to this letter, provide the following:

• A CAPA plan, based on a retrospective assessment of your cleaning and disinfection program, that includes appropriate remediations to your cleaning/disinfection processes and practices, and timelines for completion. Provide a detailed summary of vulnerabilities in your process for lifecycle management of equipment cleaning and disinfection. Describe improvements to your cleaning and disinfection program, including enhancements to cleaning effectiveness, improved ongoing verification of proper cleaning and disinfection execution for all products and equipment, and all other needed remediations.

• A comprehensive environmental monitoring program for your facility, including but not limited to, frequency, location, types, and methods of monitoring. The program should include provisions to vigilantly monitor both daily results and trends.

• A comprehensive personnel monitoring program for operators involved in aseptic processing operations.

4. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160(b)).

You failed to validate your sterility test method and also failed to use suitable media for sterility testing of your sterile injectable homeopathic drug products. Furthermore, you failed to perform endotoxin and particulate matter testing for your sterile injectable homeopathic drug products.

Your response included certificates of analysis for third-party testing of multiple products, but did not address validation of your sterility test method. The sterility testing of each batch is the last in a series of essential CGMP controls that ensure that a drug product is sterile and suitable for release.

In response to this letter, provide the following:

• A comprehensive, independent assessment of your laboratory practices, procedures, methods, equipment, documentation, and analyst competencies. Based on this review, provide a detailed plan to remediate and evaluate the effectiveness of your laboratory system.

• An update of all testing methods used by your firm and your method validation status.

Additional Guidance on Aseptic Processing

See FDA's guidance document *Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice* to help you meet the CGMP requirements when manufacturing sterile drugs using aseptic processing at https://www.fda.gov/media/71026/download (https://www.fda.gov/media/71026/download).

In addition to addressing the above CGMP violations, any drug marketed by your firm must conform with all applicable requirements of the FD&C Act, including those outlined in the Unapproved New Drug Charges section below.

Unapproved New Drugs

Statements on your firm's product inserts that establish the intended uses of your products include, but are not limited to, the following:

"Articula," "Mesenchyme," "Connectissue," "MuSkel-Neural," "Ouch," "Ithurts," "Adipose," "Systemic Detox," "Hair," "Neuro 3," "Infla," "Prolo," "Lymph 1," "GI," "Neuro," "Arthros," "Male+," "Immunexx," "Relief+," "Intra-Cell," "Facial," and "ANS/CNS"

• "[D]esigned to nourish the system."

"Collagen"

• "[I]njected into the various layers of the skin, muscles, ligaments or other body tissues where collagen support or regeneration is desired."

The above claims for "Articula," "Mesenchyme," "Connectissue," "MuSkel-Neural," "Ouch," "Ithurts," "Adipose," "Systemic Detox," "Hair," "Neuro 3," "Infla," "Collagen," "Prolo," "Lymph 1," "GI," "Neuro," "Arthros," "Male+," "Immunexx," "Relief+," "Intra-Cell," "Facial," and "ANS/CNS" demonstrate that they are drugs, as defined by section 201(g) of the FD&C Act, 21 U.S.C. 321(g), because they are intended to cure, mitigate, treat, or prevent disease and/or intended to affect the structure or function of the body of man or other animals. Moreover, these products are "new drugs," as defined by 201(p) of the FD&C Act, 21 U.S.C. 321 (p), because they are not generally recognized as safe and effective for use under the conditions prescribed, recommended, or suggested in their labeling. Under section 505(a) of the FD&C Act, 21 U.S.C. 355(a), new drugs may not be introduced or delivered for introduction into interstate commerce without prior approval from FDA. No approved application pursuant to section 505 of the FD&C Act, 21 U.S.C. 355, is in effect for these products. Accordingly, the introduction or delivery for introduction into interstate commerce of these products violates sections 301(d) and 505(a) of the FD&C Act, 21 U.S.C. 331(d) and 355(a).

We recognize that these injectable homeopathic products are labeled with active ingredients measured in homeopathic strengths. Under section 201(g)(1) of the FD&C Act, 21 U.S.C. 321(g)(1), the term "drug" includes articles recognized in the official Homeopathic Pharmacopeia of the United States (HPUS), or any supplement to it. Homeopathic drug products are subject to the same regulatory requirements as other drugs; nothing in the FD&C Act exempts homeopathic drugs from any of the requirements related to adulteration, misbranding, or approval.

Within fifteen (15) working days of receipt of this letter, specific to the violations for unapproved new drugs, please notify the Office of Unapproved Drugs and Labeling Compliance in writing of the specific steps you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the time within which you will complete the correction. Your response should be sent by email to FDAADVISORY@fda.hhs.gov.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility and in connection with your marketed products. You are responsible for investigating and determining the causes of these violations and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all requirements of federal law and FDA regulations. You should take prompt action to correct the violations cited in this letter.

FDA placed your firm on Import Alert 66-40 on October 9, 2019.

Until you correct all violations completely and we confirm your compliance with CGMP, FDA may withhold approval of any new drug applications or supplements listing your firm as a drug manufacturer.

Failure to correct these violations may also result in the FDA continuing to refuse admission of articles manufactured at 8046255 Canada Inc., dba Viatrexx, FEI 3010033797, at 1360 Rue Louis-Marchand, Beloeil into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Articles under this authority may be subject to refusal of admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351 (a)(2)(B).

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your violations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov

Please identify your response with FEI 3010033797 and ATTN: Lynnsey Renn.

Sincerely,
/S/

Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

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