DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993-0002

TO: Global Drug Supply

FROM: The United States Food and Drug Administration

RE: Shipment of Unapproved New Drugs and Misbranded Drugs to the United States

DATE: December 6th, 2016

WARNING LETTER

The United States Food and Drug Administration (FDA) has determined that your firm causes the introduction of unapproved new drugs and misbranded drugs into the United States (U.S.) by shipping to U.S. consumers in violation of sections 301(a), 301(d), and 505(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) [21 U.S.C. §§ 331(a), 331(d), and 355(a)]. FDA requests that Global Drug Supply immediately cease shipping violative drug products to U.S. consumers.

UNAPPROVED NEW DRUGS

Global Drug Supply dispenses and ships unapproved new drugs directly to individual U.S. consumers on behalf of Canadadrugs.com, an internet pharmacy from which U.S. consumers purchase violative drug products.[1] The drug products shipped by Global Drug Supply are represented as being equivalent to U.S. approved drug products that are indicated to treat serious conditions including (but not limited to) seizures, Parkinson's, hypertension, depression, and asthma. Because these products are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and/or intended to affect the structure or function of the body, these products are drugs within the meaning of section 201(g) of the FD&C Act [21 U.S.C. § 321(g)]. These products are also new drugs as defined by section 201(p) of the FD&C Act [21 U.S.C. § 321(p)] because they are not generally recognized as safe and effective for their labeled uses. New drugs may not be legally introduced or delivered for introduction into interstate commerce without prior approval from FDA as described in section 505(a) of the FD&C Act [21 U.S.C. § 355(a)]. No approved applications pursuant to section 505 of the FD&C Act [21 U.S.C. § 355] are in effect for these products. Accordingly, their introduction or delivery for introduction into interstate commerce violates sections 301(d) and 505(a) of the FD&C Act [21 U.S.C. §§ 331(d) and 355(a)].

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[1] Canadadrugs.com and Global Drug Supply are both under criminal indictment in the U.S. District Court for the District of Montana for engaging in the illegal importation of unapproved new drugs, misbranded drugs, and counterfeit drugs for sale and distribution to physicians and physician office practices in the U.S. (The charges contained in the Indictments are merely accusations and the defendants are presumed innocent unless and until proven guilty.)
Canadadrugs.com received an FDA Warning Letter in 2012 for causing the introduction of misbranded and unapproved drugs into the U.S. *See* http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm321068.htm.

FDA physically examined packages imported to the U.S. by Global Drug Supply that were determined, based on shipping labels, prescription order forms, and product labeling to contain unapproved new drugs.

One example of an unapproved new drug shipped by Global Drug Supply to a U.S. consumer is Pristiq. While Pristiq is the name of an FDA-approved prescription drug, the product labeling for the drug shipped to the U.S. from Global Drug Supply is intended for Australia. For example, the product labeling states, "Pfizer Australia Pty Ltd" and refers to medical information available at "Australia 1800 675 229" and "medicalaffairs.anzpfizer.com." In the U.S., Pristiq is approved for the treatment of depression. Shipping an unapproved version of this drug to U.S. consumers is particularly concerning given that FDA-approved Pristiq bears a boxed warning, commonly referred to as a "black box warning," which is the strongest warning FDA requires, indicating that the drug carries a significant risk of serious or even life-threatening adverse effects. The boxed warning addresses suicidal thoughts or actions. There have also been reports of several serious adverse reactions associated with the use of Pristiq such as a potentially life-threatening condition called serotonin syndrome that can happen when Pristiq is taken with certain other medicines. Serotonin syndrome can cause serious changes in how the brain, muscles, heart and blood vessels, and digestive system work. In addition, Pristiq can cause other serious side effects such as new or worsened high blood pressure, abnormal bleeding or bruising, and visual problems.

Another example of an unapproved new drug shipped by Global Drug Supply to a U.S. consumer is Exforge. While Exforge is the name of an FDA-approved prescription drug indicated for the treatment of high blood pressure, the product labeling for the drug shipped to the U.S. from Global Drug Supply states that it is distributed in Australia. Shipping an unapproved version of Exforge to U.S. consumers is especially concerning given that FDA-approved Exforge bears a boxed warning regarding harm or death to an unborn baby. Exforge product shipped to the U.S. by Global Drug Supply contains no such boxed warning. In addition, the FDA-approved product labeling for Exforge includes warnings and precautions regarding low blood pressure, risk of heart attack or worsening chest pain, decreased kidney function, and increased potassium levels in the blood. There have been reports of several adverse reactions associated with the use of Exforge including, but not limited to, swelling of the hands, ankles, or feet, nasal congestion or sore throat, head or chest cold, and dizziness.

MISBRANDED DRUGS:

Because drugs shipped by Global Drug Supply appear to be manufactured and marketed for countries other than the U.S., they are unapproved new drugs under the FD&C Act, as described above. A drug is misbranded under section 502(f)(1) of the FD&C Act [21 U.S.C. § 352(f)(1)] if the drug fails to bear adequate directions for its intended use(s). "Adequate directions for use" means directions under which a layperson can use a drug safely and for the purposes for which it is intended (21 CFR 201.5). The drug products shipped by Global Drug Supply purport to treat conditions that are not amenable to self-diagnosis and treatment by persons who are not medical practitioners. Therefore, adequate directions for use cannot be written for these drug products, and they must qualify for one of the exemptions to 502(f)(1) to avoid being misbranded The exemption

to 502(f)(1) of the FD&C Act [21 U.S.C. § 352(f)(1)] found at 21 CFR § 201.100 does not apply to unapproved new drugs because that exemption requires that such drugs bear "the labeling authorized by the approved new drug application." Furthermore, unapproved new prescription drugs also do not qualify for the exemption set forth at 21 CFR 201.115, which also requires an approved new drug application (NDA) or active investigational new drug application (IND). Consequently, a prescription drug that is a new drug and has not been approved by FDA or is not subject to an exemption from the premarketing approval requirements under the FD&C Act cannot qualify for the exemptions to 502(f)(1). Because none of the exemptions to 502(f)(1) apply, the labeling for the drug products shipped by Global Drug Supply fails to bear adequate directions for the intended uses, and the products are therefore misbranded under section 502(f)(1) of the FD&C Act [21 U.S.C. § 352(f)(1)]. By shipping these products to U.S. consumers, Global Drug Supply is causing the introduction of misbranded drugs into interstate commerce in violation of section 301(a) of the FD&C Act [21 U.S.C. § 331(a)].

Additional examples of misbranded and unapproved new drugs that have been shipped by Global Drug Supply to U.S. consumers are noted in the table below.* This list may not be all-inclusive.

Generic Name	Brand Name
Budesonide/formoterol	Vannair
Bupropion	Zyban
Celecoxib	Celebrex
Conjugated Estrogen	Premarin
Estrogens, Conjugated/Medroxyprogesterone	Premia
Duloxetine	Cymbalta
Escitalopram	Lexapro
Estradiol	Estradot
Estradiol/Norethindrone	Estalis
Ezetimibe	Ezetrol
Fexofenadine	Telfast
Finasteride	Regen
Fluticasone	Flixotide
Fluticasone/Salmeterol	Seretide
Hydroxychloroquine	Plaquenil
Metoprolol CR	Betaloc CR
Pentosan	Elmiron
Phenytoin	Dilantin
Pramipexole	Sifrol
Rosuvastatin	Crestor
Salbutamol/Ipratropium	Duolin
Sildenafil	Viagra
Tazarotene	Zorac
Telmisartan/Hydrochlrothiazide	Micardis Plus
Tretinoin	Retrieve
Valsartan/Hydrochlorothiazide	Co-Diovan

*Several of the accompanying labels purport that the shipped drug is equivalent to an FDA-approved drug.

CONCLUSION:

FDA is taking this action against Global Drug Supply because of the risks posed by its conduct in causing the importation of drugs that are unapproved and misbranded into the U.S. FDA's regulation and oversight of the drug approval process protects consumers by requiring rigorous scientific standards for new drug approval, labeling review for accuracy and completeness, and manufacturing procedures and testing performed under closely controlled conditions at FDA-registered and inspected facilities.

Unapproved foreign versions of FDA-approved drugs often have different trade names or manufacturers and may have substantially different risk profiles due to changes in drug formulations, drug delivery methods, directions for use, or contraindications and warnings. Any and all of these factors may harm consumers who are unaware that they are not receiving the same medications prescribed by their healthcare practitioners. Taking an unapproved drug in place of the FDA-approved product can negatively affect patient outcomes because the health care practitioner may unknowingly make subsequent treatment decisions based on the patient's response to the unapproved drug, rather than to the approved drug that was prescribed. This can also cause potentially dangerous drug interactions with the patient's other medications.

This letter is not intended to identify all the ways in which your activities might be in violation of law. You should promptly cease shipping misbranded and unapproved new drug products to U.S. consumers and correct any other violations of the FD&C Act. Failure to do so immediately may result in further regulatory action, including seizure or injunction, without further notice.

Please notify this office in writing within 10 working days of receipt of this letter of any steps you have taken or will take to correct the violations set forth above and to prevent their recurrence. If the corrective action(s) cannot be completed within 10 working days, state the reason for the delay and the time within which the correction(s) will be completed. Your response, and any other inquiries concerning this letter, should be sent to FDA's Internet Pharmacy Task Force at FDAInternetPharmacyTaskForce-CDER@fda.hhs.gov.

Sincerely,

/s/

Thomas Christl
Director
Office of Drug Security, Integrity, and Response
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration