DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21264/S-010

SUPPLEMENT APPROVAL

US WorldMeds, LLC
Attention: Kristen L. Gullo
Director, Strategic & Clinical Operations
4010 Dupont Circle, Suite L-07
Louisville, KY 40207

Dear Ms. Gullo:

Please refer to your Supplemental New Drug Application (sNDA) dated May 4, 2011, received May 6, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for APOKYN (apomorphine hydrochloride) injection, 10mg/mL.

We acknowledge receipt of your amendments dated June 7, 2011, March 6, 2012, and December 6, 2012.

This "Prior Approval" supplemental new drug application proposes updated formatting for compliance with the Federal Register final rule issued January 24, 2006, "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" [21 CFR 201.56 and 201.57], commonly referred to as the physician labeling rule (PLR).

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

As the agreed-upon labeling includes both a Patient Package Insert and an Instructions for Use, we refer you to 21CFR 201.56(e)(6), 201.57(c)(18) and 201.80(f)(2) and the Guidance for Industry: Labeling for Human Prescription Drug and Biological Products –Implementing the PLR Content and Format Requirements, which can be accessed from the following link: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm075082.pdf

We remind you that, as stated in the above listed references, any FDA-approved patient labeling is required to either accompany the labeling as a separate document (e.g., included in the carton with the drug) or be reprinted immediately following the last section of the labeling. You may choose the option of either reprinting the FDA-approved patient labeling immediately following the last section

of labeling or having the FDA-approved patient labeling accompany the labeling as a separate document (e.g., included in the carton with the drug).

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert and instructions for use), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments and timetables as stated in your approval letter dated April 20, 2004:

191-11 Clinical Commitment #1
You have committed to the conduct of a clinical trial designed to assess the potential effects of apomorphine on the QTc interval. Due to the complexity of the design of this study, submit the protocol for review and discussion prior to study initiation.

Protocol Submission Date: October 2004
Study Start Date: April 2005
Final Report Submission Date: October 2006

191-18 Clinical Pharmacology and Biopharmaceutics Commitment #3
You have committed to conduct a pharmacokinetic and pharmacodynamic study to assess the drug interaction potential of apomorphine with alcohol and antihypertensives to include vasodilators (including short-and long-acting nitrates).

Protocol Submission Date: September 2004
Study Start Date: December 2004
Final Report Submission Date: 6 months after study completion

Submit clinical protocols to your IND 052844 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Tracy Peters, PharmD, Senior Regulatory Project Manager, at (301) 796-2953.

Sincerely,

{See appended electronic signature page}

Eric Bastings, M.D.
Deputy Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC P BASTINGS
07/25/2014