



NDA 021264/S-016

## SUPPLEMENT APPROVAL

US WorldMeds, LLC  
Attention: Melissa Bateson  
Senior Manager, CMC Regulatory  
4441 Springdale Road  
Louisville, KY 40241

Dear Ms. Bateson:

Please refer to your supplemental new drug application (sNDA) dated and received November 20, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Apokyn (apomorphine hydrochloride injection), 10mg/mL.

This Prior Approval supplemental new drug application provides for labeling changes pursuant to the Fulfillment of Postmarketing Commitment (PMC) 191-18: "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)".

The supplemental new drug application proposes labeling changes in the Warnings and Precautions subsection 5.4 (Syncope/ Hypotension/Orthostatic Hypotension), Drug Interactions subsections 7.2 and 7.3 (Antihypertensive Medications and Vasodilators; Alcohol), Clinical Pharmacology subsections 12.2 and 12.3 (Pharmacodynamics; Pharmacokinetics), and the Patient Counseling Information section of the Prescribing Information. The supplemental new drug application also proposes updates in the Patient Information, and labeling revisions based on labeling requirements in the Code of Federal Regulations (21 CFR 201.57) and recommendations in labeling Guidances.

(b) (4)

### **APPROVAL & LABELING**

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

## **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 FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Information, 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 *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include 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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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).

## **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 Jack Dan, Regulatory Project Manager, at (240) 402-6940.

Sincerely,

*{See appended electronic signature page}*

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

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

ENCLOSURE(S):

- Content of Labeling  
Prescribing Information  
Instructions for Use

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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ERIC P BASTINGS  
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