



NDA 017812/S-034  
NDA 018421/S-033  
NDA 018558/S-028

## **SUPPLEMENT APPROVAL**

Hikma Pharmaceuticals USA Inc.  
Attention: Chrysoula Koukoutsis  
Associate Director, Drug Regulatory Affairs  
1809 Wilson Road  
Columbus, OH 43228

Dear Mr. Koukoutsis:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received December 16, and 17, 2019, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lithium Carbonate Capsules (NDA 017812), Lithium Carbonate Tablets (NDA 018558), and Lithium Oral Solution (NDA 018421).

We also refer to our letter dated December 5, 2019, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for lithium. This information pertains to the risk of drug reaction with eosinophilia and systemic symptoms (DRESS).

These supplemental new drug applications provide for revisions to the labeling for Lithium consistent with our December 5, 2019, letter.

### **APPROVAL & LABELING**

We have completed our review of these applications. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

We note that your December 16, and 17, 2019, submissions include final printed labeling (FPL) for your Prescribing Information, and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this FPL is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

### **WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

## **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 and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (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).

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 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.

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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>.

## **PROMOTIONAL MATERIALS**

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 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, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.

## **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 Ermias Zerislassie, Safety Regulatory Project Manager, at (301) 796-2770.

Sincerely,

*{See appended electronic signature page}*

Tiffany R. Farchione, MD  
Director (Acting)  
Division of Psychiatry  
Office of Neuroscience  
Center for Drug Evaluation and Research

### ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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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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