

NDA 050786/S-023

## SUPPLEMENT APPROVAL

Allergan Sales, LLC  
Attention: Linda Kunka, MA  
Director, Regulatory Affairs  
5 Giralda Farms  
Madison, NJ 07940

Dear Ms. Kunka:

Please refer to your supplemental new drug application (sNDA) dated and received November 03, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for PYLERA (bismuth subcitrate potassium, metronidazole, tetracycline hydrochloride) Capsules.

We also refer to our letter dated October 07, 2020, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for metronidazole. This information pertains to the risk of QT prolongation.

This supplemental new drug application provides for revisions to the labeling for PYLERA (bismuth subcitrate potassium, metronidazole, tetracycline hydrochloride) Capsules.

The agreed upon changes to the language included in our October 07, 2020 letter are as follows (additions are noted by underline and deletions are noted by ~~strikethrough~~).

### 5 WARNINGS AND PRECAUTIONS

#### 5.14 Drug Interactions

##### Drugs that Prolong the QT interval

QT prolongation has been reported with metronidazole, a component of PYLERA, particularly when administered with drugs with the potential for prolonging the QT interval.

### 6 ADVERSE REACTIONS

#### 6.3 Other Important Adverse Reactions from Labeling for the Individual Components of PYLERA

Metronidazole

Cardiac disorders : QT <sup>(b) (4)</sup> prolongation has been reported, particularly when metronidazole was administered with drugs with the potential for prolonging the QT interval. Flattening of the T-wave may be seen in electrocardiographic tracings.

## **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](http://FDA.gov).<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information), 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. If the content of labeling in SPL format initially submitted with this CBE-0 labeling supplement is identical to the attached approved labeling, an additional submission of content of labeling in SPL format is not required.

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).

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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>.

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).

### **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 Carmen DeBellas, Chief, Regulatory Project management Staff, at 301-796-1203.

Sincerely,

*{See appended electronic signature page}*

Sumathi Nambiar, MD, MPH  
Director  
Division of Anti-Infectives  
Office of Infectious Diseases  
Center for Drug Evaluation and Research

#### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information

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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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SUMATHI NAMBIAR  
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