

# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

### ***APPLICATION NUMBER:***

**NDA 019591/S-030**

***Trade Name:*** Lariam for oral use, 250mg

***Generic or Proper Name:*** Mefloquine Hydrochloride

***Sponsor:*** Hoffman-LaRoche, Inc.

***Approval Date:*** April 29, 2011

***Indication:*** Indicated for the treatment of mild to moderate acute malaria caused by mefloquine-susceptible strains of *P. falciparum* (both chloroquine-susceptible and resistant strains) or by *Plasmodium vivax*.

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**NDA 019591/S-030**  
**CONTENTS**

**Reviews / Information Included in this NDA Review.**

<b>Approval Letter</b>	<b>X</b>
<b>Other Action Letters</b>	
<b>Labeling</b>	
<b>REMS</b>	<b>X</b>
<b>Summary Review</b>	
<b>Officer/Employee List</b>	
<b>Office Director Memo</b>	
<b>Cross Discipline Team Leader Review</b>	
<b>Clinical Review(s)</b>	
<b>Product Quality Review(s)</b>	
<b>Non-Clinical Review(s)</b>	
<b>Statistical Review(s)</b>	
<b>Clinical Microbiology / Virology Review(s)</b>	
<b>Clinical Pharmacology Review(s)</b>	
<b>Other Reviews</b>	
<b>Risk Assessment and Risk Mitigation Review(s)</b>	
<b>Proprietary Name Review(s)</b>	
<b>Administrative/Correspondence Document(s)</b>	

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*APPLICATION NUMBER:*

**NDA 019591/S-030**

**APPROVAL LETTER**



NDA 19591/S-030

**SUPPLEMENT APPROVAL  
RELEASE REMS REQUIREMENT**

Hoffmann-La Roche Inc.  
Attention: Ms. Lynn DeVenezia-Tobias  
Senior Program Manager, Diversified Products  
340 Kingsland Street  
Nutley, NJ 07110-1199

Dear Ms. DeVenezia-Tobias:

Please refer to your Supplemental New Drug Application (sNDA) dated March 31, 2011, received April 1, 2011, under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lariam<sup>®</sup> (mefloquine hydrochloride) Tablets, 250 mg.

We also acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment dated January 20, 2011.

This supplemental new drug application proposes that the requirement for the Lariam REMS be eliminated.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter.

**RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for Lariam<sup>®</sup> (mefloquine hydrochloride) was originally approved on August 20, 2009. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

You propose that FDA no longer require a REMS for Lariam<sup>®</sup> (mefloquine hydrochloride).

We have determined that it is no longer necessary to include the Medication Guide as an element of the approved REMS, and that a REMS is no longer necessary to ensure that the benefits of the Lariam<sup>®</sup> (mefloquine hydrochloride) outweigh its risks. Therefore, we agree with your proposal and a REMS for Lariam<sup>®</sup> (mefloquine hydrochloride) is no longer required. We remind you that the Medication Guide will continue to be part of the approved labeling in accordance with 21 CFR 208.

## **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  
Division of Drug Marketing, Advertising, and Communications  
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 Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

## **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 Gregory DiBernardo, Regulatory Project Manager, at (301) 796-4063.

Sincerely,

*{See appended electronic signature page}*

Ozlem Belen, MD, MPH  
Deputy Director for Safety  
Division of Special Pathogen and Transplant Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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OZLEM A BELEN  
04/29/2011

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***APPLICATION NUMBER:***

**NDA 019591/S-030**

**REMS**

**Risk Evaluation and Mitigation Strategy (REMS) Memorandum**  
**REMS Elimination**

**U.S. FOOD AND DRUG ADMINISTRATION**  
**CENTER FOR DRUG EVALUATION AND RESEARCH**  
**Office of Antimicrobial Products**  
**Division of Special Pathogen and Transplant Products**

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<b>NDA/BLA #s:</b>	19591
<b>Products:</b>	Lariam <sup>®</sup> (mefloquine hydrochloride)
<b>APPLICANT:</b>	Hoffmann-La Roche Inc.
<b>FROM:</b>	Ozlem Belen, MD, MPH Deputy Director for Safety
<b>DATE:</b>	April 15, 2011

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A risk evaluation and mitigation strategy (REMS) for Lariam<sup>®</sup> (mefloquine hydrochloride) was approved on August 20, 2009 to ensure the benefits of the drug outweigh the risk resulting from an interaction between Lariam<sup>®</sup> (mefloquine hydrochloride) and ketoconazole. The risk of potentially fatal prolongation of QTc is increased if ketoconazole is taken during Lariam<sup>®</sup> (mefloquine hydrochloride) therapy. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

On March 31, 2011, Hoffmann-La Roche submitted a proposed REMS modification to release the requirement for the REMS. The REMS modification referenced a REMS assessment dated January 20, 2011.

After consultations between the Office of New Drugs (OND) and the Office of Surveillance and Epidemiology (OSE), we have determined a REMS is no longer necessary to ensure the benefits of the drug outweigh the risk described above because labeling is adequate to describe the risks. The Medication Guide will continue to be part of the approved labeling in accordance with 21 CFR 208. Like other labeling, Medication Guides are subject to the safety labeling change provisions of section 505(o)(4) of the FDCA.



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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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HYUN J SON  
04/29/2011

OZLEM A BELEN  
04/29/2011