CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-268

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	November 25, 2008
To:	Renata, Albrecht, M.D., Director **Division of Special Pathogen and Transplant Products**
Through:	Jodi Duckhorn, M.A., Team Leader **Patient Labeling and Education Team** **Division of Risk Management (DRISK)**
From:	LaShawn Griffiths**,** MSHS-PH, BSN, RN Patient Product Information Reviewer **Patient Labeling and Education Team** **Division of Risk Management (DRISK)**
Subject:	Review of Patient Labeling
Drug Name(s) and Application Numbers:	NDA 22-268 Coartem (artemether and lumefantrine) tablets
Applicant/sponsor:	Novartis Pharmaceuticals
OSE RCM #:	2008-1723

1 INTRODUCTION

Novartis Pharmaceuticals submitted a New Drug Application NDA 22-268 for Coartem tablets on June 27, 2008. The submission includes proposed Professional Information (PI) in PLR format, with Patient Labeling Information (Patient Package Insert) included in section 17 Patient Counseling Information. Coartem is indicated for treatment of malaria in patients of 5kg body weight and above with acute, uncomplicated infections due to *Plasmodium falciparum* or mixed infections including *P. falciparum*. Coartem has been shown to be effective in geographical regions where resistance to chloroquine has been reported.

The review division requested that DRISK review the sponsor's proposed patient labeling. This review is written in response to that request.

2 MATERIAL REVIEWED

- Coartem Professional Information (PI) submitted by sponsor on June 27, 2008 and further revised by the Review division throughout the review cycle.
- Coartem Patient Package Insert (PPI) submitted by sponsor on June 27, 2008.

3 DISCUSSION

The purpose of patient directed labeling is to facilitate and enhance appropriate use and provide important risk information about medications. Our recommended changes are consistent with current research to improve risk communication to a broad audience, including those with lower literacy.

The draft PPI submitted by the sponsor has a Flesch Kinkaid grade level of 7.4 and a Flesch Reading Ease score of 62.5%. To enhance patient comprehension, materials should be written at a 6^{th} to 8^{th} grade reading level, and have a reading ease score of at least 60% (60% corresponds to an 8^{th} grade reading level). The scores as submitted by the sponsor are acceptable.

In our review of the PPI we have:

- simplified wording and clarified concepts where possible,
- ensured consistency with the PI,
- removed unnecessary or redundant information
- Ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006).

In 2008, The American Society of Consultant Pharmacists Foundation in collaboration with The American Foundation for the Blind published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. They recommend using fonts such as Arial, Verdana, or APHont to make medical information more accessible for patients with low vision. We recommend that the Sponsor reformat the PPI using the font APHont, which was developed by the American Printing House for the Blind specifically for low vision readers.

All future relevant changes to the PI should also be reflected in the PPI.

4 CONCLUSIONS AND RECOMMENDATIONS

1. The sponsor uses the term [redacted] in the proposed PPI. [redacted] is vague and less commonly understood. We have changed this term throughout the PPI to "healthcare provider."
2. In the section, "How should I take Coartem?":
   - we removed the verbose and potentially confusing instruction that read, [redacted] We added a day- by- day dosing regimen as this provides clarity and reduces patient confusion.
   - we recommend adding an instruction to use water that has been boiled due to possible water contamination. If an instruction to boil the water will be added to the PPI, it must be added to the PI for consistency. The PPI must be consistent with the PI.
3. We added a "What are the ingredients in Coartem?" section and listed the active and the inactive ingredients to the end of the PPI. This is a standard section in patient labeling.
4. In the section, "How should I store Coartem?," we have deleted [redacted] as it is more realistic to provide the acceptable temperature storage range.
5. In the section "What are the possible side effects of Coartem?" we bulleted the side effects as bullets are easier to read.
6. Contractions should not be used in patient information as they are generally not understood at lower reading levels. Sponsor uses the contraction "doesn't." This was replaced with "does not."
7. We have added the statement:

   > Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

   This verbatim statement is required for all Medication Guides effective January 2008 (see 21 CFR 208.20 (b)(7)(iii); also see Interim Final Rule, *Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products* in Federal Register Vol. 73, No. 2, p.402-404, 1/3/2008). Although, not required for voluntary patient information, like Coartem, we recommend adding this statement to all FDA-approved patient labeling for consistency.

Please contact us if you have any concerns or questions.

10 Page(s) Withheld

_____ Trade Secret / Confidential

X Draft Labeling

_____ Deliberative Process

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

/s/

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11/26/2008 12:17:32 PM
DRUG SAFETY OFFICE REVIEWER

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