DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-078/S-014

GlaxoSmithKline
Attention: Debra Hackett
Director, US Regulatory Affairs
One Franklin Plaza
200 N. 16th Street, FP1005
Philadelphia, PA 19102

Dear Ms. Hackett:

Please refer to your supplemental new drug application dated November 15, 2006, received November 17, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Malarone ® (atovaquone and proguanil hydrochloride) Tablets.

We acknowledge receipt of your submissions dated August 6, 2007, October 10, 2007, and January 29, 2008.

This supplemental new drug application provides for the following revisions to the package insert (additions are indicated by underlined):

1. The following text was added as the fifth paragraph under **CLINICAL PHARMACOLOGY/ Drug Interactions** subsection:

   Concomitant administration of atovaquone (750 mg BID with food for 14 days) and indinavir (800 mg TID without food for 14 days) did not result in any change in the steady-state AUC and C_{max} of indinavir but resulted in a decrease in the C_{trough} of indinavir (23% decrease [90% CI 8%, 35%]). Caution should be exercised when prescribing atovaquone with indinavir due to the decrease in trough levels of indinavir.

2. The following text was added as the third paragraph under the **PRECAUTIONS/ Drug Interactions** subsection:

   Proguanil may potentiate the anticoagulant effect of warfarin and other coumarin-based anticoagulants. The mechanism of this potential drug interaction has not been established. Caution is advised when initiating or withdrawing malaria prophylaxis or treatment with MALARONE in patients on continuous treatment with coumarin-based anticoagulants. When these products are administered concomitantly, suitable coagulation tests should be closely monitored.

We have completed the review of this supplemental new drug application, as amended. Accordingly, this supplemental application is approved effective on the date of this letter, for use as in the agreed labeling text submitted on January 29, 2008.

If you have any questions, call Christine Lincoln, RN, M.S., MBA, Regulatory Health Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office Antimicrobial Products
Center for Drug Evaluation and Research

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

/s/

Renata Albrecht

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