DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-078/S-007

GlaxoSmithKline
Attention: Ms. Debra Hackett
Regulatory Affairs
One Franklin Plaza
P.O. Box 7929
Philadelphia, PA 19101-7929

Dear Ms. Hackett:

Please refer to your supplemental new drug application (sNDA) dated May 27, 2004, received May 28, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for for Malarone®(atovaquone and proguanil hydrochloride) Tablets, 250 mg/100 mg and 62.5 mg/25 mg.

This "Changes Being Effected" supplemental new drug application provides for the following revisions to the Malarone® package insert (PI):

Added text = double underline and Deleted text = ~~strikethrough~~

ADVERSE REACTIONS

Post-Marketing Adverse Reactions: In addition to adverse events reported from clinical trials, the following events have been identified during world-wide post-approval use of MALARONE. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to MALARONE.

> ***Skin:*** Cutaneous reactions ranging from rash, photosensitivity, and urticaria to rare cases of erythema multiforme and ~~. In addition, one case of~~ Stevens-Johnson syndrome ~~has been reported~~.
>
> ***Central Nervous System:*** Rare cases of seizures and psychotic events (such as hallucinations); however, a causal relationship has not been established.

We have completed our review of this application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text (enclosed). Accordingly, this supplemental application is approved on the date of this letter.

The final printed labeling (FPL) must be identical to the agreed upon labeling (text for the package insert submitted May 27, 2004).

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: ***Providing Regulatory Submissions in Electronic Format - NDAs*** (January 1999) and ***Providing Regulatory Submissions in Electronic Format – Content of Labeling*** (February 2004). The guidances specify that labeling to be submitted in *pdf* format. To assist in our review of the FPL and future submission, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. For administrative purposes, this submission should be designated "**FPL for approved supplement NDA 21-078/S-007**." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Yon Yu, Pharm D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
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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