September 6, 2001

GlaxoSmithKline

IMPORTANT CORRECTION OF DRUG INFORMATION

GlaxoSmithKline
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Dear Healthcare Provider:

This letter is being sent to you at the request of the U.S. Food and Drug Administration (FDA). The FDA's Division of Drug Marketing, Advertising and Communications (DDMAC) has notified GlaxoSmithKline (GSK) that statements and other actions by GSK concerning Avandia® (rosiglitazone maleate) tablets, were false or misleading and in violation of the Federal Food, Drug, and Cosmetic Act.

Specifically, the FDA has objected to oral statements by representatives of GSK, at a recent national meeting of endocrinologists, denying the existence of important new risk information in the product label of *Avandia*. This new risk information includes a warning concerning the risk of heart failure and other cardiovascular adverse events seen in patients taking *Avandia* in combination with insulin, and a precaution concerning postmarketing reports of serious hepatic events in patients taking *Avandia*. The FDA has also objected to GSK's dissemination of promotional materials for *Avandia* that failed to disclose the important new risk information. Therefore, the FDA has requested that GSK correct these false and misleading promotional messages accordingly.

On February 8, 2001, the FDA approved revisions to the *Avandia* product labeling (prescribing information or PI). Among the changes is a new warnings section that includes:

- *Avandia*, like other thiazolidinediones, alone or in combination with other antidiabetic agents, can cause fluid retention, which may exacerbate or lead to heart failure.
- Patients should be observed for signs and symptoms of heart failure. *Avandia* should be discontinued if any deterioration in cardiac status occurs.
- The results of two controlled studies showed an increased risk of heart failure and other cardiac adverse events in patients taking both *Avandia* and insulin, compared with those taking placebo and insulin. Some patients who developed heart failure on *Avandia* plus insulin combination therapy had no known prior evidence of congestive heart failure, or pre-existing cardiac failure. ***Avandia* is not indicated for combination therapy with insulin.**

There is also new language regarding postmarketing reports of serious hepatic events in patients taking *Avandia*, as follows:

(over)

- In postmarketing experience with *Avandia*, reports of hepatitis and of hepatic enzyme elevations to three or more times the upper limit of normal have been received. Very rarely, these reports have involved hepatic failure with and without fatal outcome, although causality has not been established.

It is important that you forward any adverse event information associated with the use of *Avandia* to GlaxoSmithKline at 1-800-366-8900. You can also report this information directly to the FDA via the MedWatch system at 1-800-FDA-1088, by fax at 1-800-FDA-0178, by mail (using a postage-paid form), or by the Internet at www.FDA.gov/medwatch.

Enclosed, for your information, is a copy of the package insert for *Avandia*.

Sincerely,

David M. Stout
President, U.S. Pharmaceuticals
GlaxoSmithKline

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