SB
SmithKline Beecham
Pharmaceuticals

March 2000

Dear Healthcare Professional:

Effective immediately, SmithKline Beecham Pharmaceuticals (SB) and Scios, Inc. will distribute Eskalith CR® (lithium carbonate) controlled release 450 mg tablets from an alternate manufacturing facility. The previously approved manufacturing facility is no longer producing *Eskalith CR* 450 mg tablets. Product produced at the new facility has been shown to be bioequivalent to *Eskalith CR* 450 mg tablets manufactured at the previously approved site; however, long-term stability data is still being collected on this product.

Long-term stability data are necessary to show that the tablets will still effectively dissolve in the GI tract after they have been stored for a period of time. Collection of these data is a standard practice in obtaining FDA approval for new sites of manufacture and in determining acceptable shelf-life for drug products.

Without long-term stability data, we cannot be certain that *Eskalith CR* 450 mg tablets manufactured at the new facility will adequately release lithium after being stored. At the present time, valid stability data have been generated for *Eskalith CR* 450 mg tablets for only two months of storage in current packaging.

Because of diminishing inventories of the current *Eskalith CR* 450 mg tablets, and public health concerns surrounding a potential out-of-stock situation, the FDA has not restricted the distribution of the product prior to the availability of full stability information; however, FDA has required that the new packages carry a shorter, provisional expiration date of 6 months.

The primary purpose of this communication is to provide you with this important information about *Eskalith CR* 450 mg tablets and to recommend certain practices to assist healthcare professionals in maintaining their patients on appropriate medication. Specifically, we suggest the following:

- Limit prescriptions of *Eskalith CR* 450 mg tablets to quantities of no more than 30 days (refill prescriptions should be filled with the most recently manufactured product available).
- Be aware of alternative medications and/or other formulations of lithium to treat manic depressive illness.
- Be aware that, as with any lithium formulation, peak serum levels may vary between individuals despite the administration of equivalent doses.
- Furthermore, since peak serum concentrations may be associated with the occurrence of adverse events, it is important to closely monitor blood levels when initiating and changing therapeutic regimens.

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One Franklin Plaza, PO Box 7929, Philadelphia, PA 19101 Telephone (215) 751 4000 Fax (215) 751 3400

SB is continuing its efforts to collect additional manufacturing stability data, and is confident that, in time, sufficient data will become available to extend the product expiry dating accordingly. However, should the product from the new facility fail its stability testing, it will be recalled.

Follow-up notices will be forthcoming as additional information becomes available. Please see the prescribing information enclosed.

If you have any questions please call (800) 366-8900 x5231.

Sincerely,

Rajinder Kumar, M.D.
SmithKline Beecham Pharmaceuticals
Vice President, Clinical Research and Development, North America

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