DRUG WARNING

IMPORTANT—FOR IMMEDIATE READING

DOSAGE—PRECAUTIONS AND CONTRAINDICATIONS IN CHOLECYSTOGRAPHY

E-FOUGERA & CO., INC.,
Hicksville, N.Y., March 1963.

DEAR DOCTOR: Recent reports have described the occurrence of certain severe side effects following the administration of more than 4.5 gm. of Orabilex (bunamiodyl sodium). Dosage recommendations and precautions have been revised as follows:

1. Repeat doses (that is, more than 4.5 gram) of Orabilex may be associated with the development of oliguria, renal tubular necrosis, and death. Use of other cholecystographic agents within one week after Orabilex ingestion may be dangerous and even fatal.

2. Orabilex is contraindicated in patients with a history of renal disease, or in the presence of any symptoms or signs suggestive of renal disease or dysfunction. Evaluation of renal function should be performed preparatory to the use of Orabilex.

A revised package brochure is enclosed for your review.

The mechanism by which multiple doses of cholecystographic media may contribute to renal embarrassment is not known.

Continuing clinical and laboratory investigations bearing on this problem are in progress. We would appreciate the submission of reports of side effects or adverse reactions following the use of Orabilex or other cholecystographic media at your earliest convenience.

Sincerely yours,

F. J. SANEN, M.D.,
Medical Director.

DRUG WARNING LETTER

SANDOZ PHARMACEUTICALS,
Hanover, N.J., March 8, 1963.

DEAR DOCTOR: In accordance with our desire to keep you up-to-date with the latest information on all our products, complete product information on Torecan is enclosed. The purpose of this letter is to draw your attention to certain modifications in indications and precautions which under FDA regulations are considered "changes in labeling." *Torecan* (*thiethylperazine*) has been on the market as an antiemetic and antinauseant since September, 1961. In the course of its broader therapeutic application, some aspects associated with its clinical use have emerged with greater clarity.

In common with other phenothiazines, Torecan may produce extrapyramidal stimulation (pseudo-parkinsonism) with the varied symptom complex characteristic of this complication. As this is more likely to occur in children and young women, Torecan is contraindicated in children under twelve years of age and in pregnancy.

Extrapyramidal effects may be manifested as a dystonic reaction (e.g. torticollis, dysphagia, oculogyric crisis, convulsion), akathisia or as pseudo-parkinson syndrome. When seen for the first time, such reactions may be mistakenly diagnosed as tetanus, hysteria, encephalitis, etc. While the syndrome is self-limiting if therapy is stopped, the clinical course may be curtailed by the administration of sedatives, anti-parkinson agents or intravenous injection of caffeine and sodium benzoate. Diphenhydramine hydrochloride intravenously has also been reported to bring relief of these symptoms.

When used as an antiemetic against vomiting induced by anesthesia, occasional instances of moderate hypotension have occurred within one-half hour of administration. This has also been reported with other phenothiazine-type antiemetics, but unlike other phenothiazines, no case of delayed hypotension has been reported with Torecan.

Restlessness and postoperative depression have not been a serious problem, but the possible development of other known reactions to the phenothiazine-antiemetics must be borne in mind.