The ad emphasizes the low incidence of certain less serious side effects such as amenorrhea, breakthrough bleeding, weight gain, etc. However, it fails to give adequate emphasis to more serious known side effects—or adequate emphasis to the possible occurrence of thrombophlebitis, pulmonary embolism or cerebral vascular accident.

The FDA points out that the pregnancy rates claimed in the ad were incorrectly based on 1065 women instead of only 880, and that the ad improperly features a pregnancy rates of 0.2 per 100 women-years. While available data do not provide a reliable scientific basis for a statement of true pregnancy rates, experience reported to us shows that the unadjusted rate for all women who were given Oracon was 2.0 per 100 women-years. The rate of 0.2 used in the ad included only those patients who insisted that they had adhered to the regimen.

Questran®

The FDA considers the summary of warning information in the journal advertisement for Questran to be inadequate in that it did not contain any information on precautions and warnings. We have attached a revised "Brief Summary," which contains the omitted precautions and warning information in capital letters.

We are discontinuing the ads in question, and future advertising will incorporate the above corrections. The safety and effectiveness of Oracon and Questran are not in question when the drugs are used in accordance with the official package inserts.

Sincerely,

P. A. WALTER, M.D.,
Director, Medical Research Department.

(NOTE.—This revised "Brief Summary," for use in medical journal advertising, contains additional information, in capital letters, taken from the official package insert.)

BRIEF SUMMARY OF WARNING INFORMATION FOR QUESTRAN® (CHOLESTYRAMINE)

Indication—Questran relieves pruritus associated with partial biliary obstruction.

Contraindication—Patients with complete biliary obstruction.

Warning—ALWAYS ADMIX QUESTRAN WITH WATER OR OTHER FLUIDS BEFORE INGESTING. TO PREVENT DEFICIENCIES OF VITAMINS A, D AND K, SUPPLEMENT THE DIET, AND SEE PRECAUTIONS BELOW.

Usage in Pregnancy—THE SAFE USE OF QUESTRAN BY PREGNANT AND LACTATING WOMEN HAS NOT BEEN ESTABLISHED.

Precautions—WITH PROLONGED QUESTRAN ADMINISTRATION, GIVE VITAMINS A AND D DAILY. INCREASED BLEEDING TENDENCIES MAY DEVELOP. PROMPT RESPONSE TO PARENTERAL VITAMIN K_1 MAY BE ANTICIPATED. ADMINISTER CHLOROTHIAZIDE, PHENYLBUTAZONE OR WARFARIN ONE HOUR BEFORE QUESTRAN. AS A PRECAUTIONARY MEASURE, ADMINISTER ALL OTHER DRUGS 30 MINUTES TO 1 HOUR BEFORE QUESTRN. A THEORETICAL POSSIBILITY EXISTS THAT PROLONGED USE MAY LEAD TO DEVELOPMENT OF HYPERCHOLOREMIC ACIDOSIS. HERE IS NO ESTABLISHED RATIONALE FOR USE OF QUESTRAN IN THE RELIEF OF PRURITUS ASSOCIATED WITH OTHER DISEASE PROCESSES.

Adverse reactions

Gastrointestinal and Dermatological—Constipation, diarrhea, nausea, gastrointestinal distress, and vomiting have been reported by about 20% of patients using cholestrymine. Reported less frequently were ABDOMINAL PAIN AND DISTENTION, rash, irritation of the skin, tongue and perianal area.

Bleeding—In 1% of patients, increased bleeding tendencies occurred due to hypoprothrombinemia.

Steatorrhea—Steatorrhea occurred but rarely, and then on doses in excess of 24 grains per day.

Cholesterol—In patients with pruritus associated with partial biliary obstruction, serum cholesterol levels usually decreases during Questra therapy. (Clinical experience has not established the therapeutic use of Questran to reduce serum chlosterol.)

Biliary Calcification—Two possible instances have been observed, but a casual relationship has not been established.