

WINTHROP LABORATORIES,
NEW YORK, N.Y.

IMPORTANT DRUG PRECAUTIONS

DEAR DOCTOR: The recent experience of various investigators has shown that Aralen® (brand of chloroquine), used alone or as an adjunct to other drugs and therapeutic measures, may be very helpful in the management of patients with lupus erythematosus or rheumatoid arthritis. Although many physicians have found that the incidence of serious side effects is lower than that encountered with other potent agents that are often employed in such patients, certain ocular complications have sometimes been reported during prolonged daily administration of chloroquine. Therefore, when chloroquine or any other antimalarial compound is to be given for long periods, it is essential that measures be taken to avoid or minimize these complications.

Thus initial and periodic (trimonthly) ophthalmologic examinations (including expert slit-lamp, fundus and visual field studies) should be performed. The initial examination will reveal if any visual abnormalities, either coincidental or due to the disease, are present and will establish a base line for further assessment of the patient's vision. Should corneal changes occur (which are thought to be reversible and which sometimes even fade on continuance of treatment), the advantages of withdrawing the drug must be weighed in each case against the therapeutic benefits that may accrue from continuation of treatment (sometimes a severe relapse follows withdrawal). If visual disturbances occur—which are not fully explainable by difficulties of accommodation or corneal opacities—and particularly if there is any suggestion of visual field restriction or retinal change, administration of the drug should be stopped immediately and the patient closely observed for possible progression.

We should like to request your cooperation in reporting to Winthrop Laboratories or to the Food and Drug Administration any patients in your own practice who have developed impairment of vision or retinal change during or subsequent to the administration of chloroquine.

A reference card of a convenient size for filing is enclosed. It contains information on the various indications for Aralen (including lupus erythematosus, rheumatoid arthritis, malaria and amebiasis), dosage, side effects and precautions.

Very truly yours,

E. J. FOLEY, M.D.,
Vice President, Medical Director.

PARKE, DAVIS & Co.,
DETROIT, MICH.

DRUG WARNING—ZARONTIN

DEAR DOCTOR: In conformance with our policy to inform physicians promptly of adverse or unusual effects from our products, and in co-operation with the Food and Drug Administration, we are calling attention to several reports received recently Zarontin® (ethosuximide).

Several cases of agranulocytosis and severe pancytopenia have been reported. Recently two cases (one fatal) of bone marrow depression have been received. These reports came from Europe; and even though many details are not known, the following information was supplied to our representatives.

Case I. Patient was a 15-year-old female with a history of having received Zarontin for four years in a dosage range from 7 to 10 capsules daily. The diagnosis was agranulocytosis and marrow transplants were not successful.

Case II. Patient was a 15-year-old male who developed increasing pallor and bleeding from the nose during the autumn of 1961 while receiving Zarontin and phenobarbital. A severe anemia (hemoglobin 5.1 Gm.), leukopenia (2480) with a pronounced granulocytopenia, and a severe thrombocytopenia were found. Zarontin was discontinued. The patient received a blood transfusion, and a bone marrow aspiration on October 20, showed hyperplasia with increased erythropoiesis and many immature red cells. During the next two months he received seven blood transfusions and 25 mg. of prednisone daily and penicillin prophylactically. The thrombocytopenia and granulocytopenia persisted and on February 2, 1962, a splenectomy was performed. During the following four months transfusions were not necessary, but the platelets and granulocytes remained low. After two transfusions the hemoglobin began to increase, reticulocytosis