Note: SOME STRAINS OF STAPHYLOCOCCI, STREPTOCOCCI, PNEUMOCOCCI, E. COLI, AND SHIGELLAE HAVE SHOWN RESISTANCE TO TETRACYCLINES. MICROORGANISMS THAT HAVE BECOME INSENSITIVE TO ONE TETRACYCLINE INVARIABLY EXHIBIT CROSS-RESISTANCE TO OTHER TETRACYCLINES, AND TETRACYCLINE RESISTANT GRAM NEGATIVE BACILLI MAY SHOW CROSS RESISTANCE TO CHLORAMPHENICOL. THEREFORE, INDICATED LABORATORY STUDIES, INCLUDING SENSITIVITY TESTS, SHOULD BE PERFORMED.

Side Effects: ANOREXIA, EPIGASTRIC DISTRESS, NAUSEA, VOMITING, BULKY LOOSE STOOLS, DIARRHEA, STOMATITIS, GLOSSITIS, ENTEROCOLITIS, PROCTITIS, PRUITUS ANI, BLACK HAIRY TONGUE, SORE THROAT, DYSPHAGIA, HOARSENESS, MACULOPAPULAR AND ERYTHEMATOUS RASHES, A RARE CASE OF EXFOLIATIVE DERMATITIS, rarely PHOTOSENSITIVITY, rarely ONYCHOLYSIS AND NAIL DISCOLORATION, DOSE-RELATED BUN RISE, URTICARIA, SERUM SICKNESS-LIKE REACTIONS, ANGIONEUROTIC EDEMA, ANAPHYLAXIS, BULGING FONTANELS IN INFANTS, DENTAL STAINING (see Precautions), TOOTH-ENAMEL HYPOPLASIA IN CHILDREN, ANEMIA, THROMBOCYTOPENIC PURPURA, NEUTROPEIA, EOSINOPHILIA, AND RARELY CHOLESTASIS ASSOCIATED WITH HIGH DOSAGE, URNARY NITROGEN LOSS WHICH MAY RESULT IN NEGATIVE NITROGEN BALANCE AND INCREASED SODIUM EXCRETION, DELAYED BLOOD COAGULATION, AND DEVELOPMENT OF PEPTIC ULCERS AND BLEEDING IN UREMIC PATIENTS. IF ALLERGIC REACTIONS OCCUR, OR IF AN INDIVIDUAL IDIOSYNCRASY APPEARS, TETRACYCLINE THERAPY SHOULD BE DISCONTINUED.

ORGANON, INC.,
West Orange, N.J., October 27, 1967.

DEAR DOCTOR: The Food and Drug Administration has requested that we call your attention to the monographs for Cortophin® Gel, Cortrophin® Zinc, Hexadrol® Phosphat Injection and Hexadrol® Tablets and Elixir in the current *Physicians Desk Reference.* The FDA considers these monographs to be incomplete in presenting necessary information for the safe and effective use of these drugs, and, therefore, potentially misleading.

To provide you with the necessary information, we enclose revised monographs for insertion in your *PDR.* The nature and extent of the additions and other revisions in the enclosed monographs are emphasized by the use of italics.

Sincerely yours,

JOSEPH D. CUONO, M.D.,
Director, Professional Services.

(NOTE.—Prescribing information for Cortrophin® Gel, Cortrophin® Zinc, Hexadrol® and Hexadrol® Phosphate Injection, which appears on pages *898–899* of your 1967 *PDR,* has been revised and is completely replaced by the following. The nature and extent of the additions and other revisions in the monographs are emphasized by use of italics.)

ORGANON, INC., WEST ORANGE, N.J.

PURIFIED CORTROPHIN® GEL

Repository Corticotropin Injection U.S.P.

Purified Cortrophin Gel is purified corticotropin (ACTH) in a sterile solution of gelatin for prolonged activity. It is supplied in two strengths: 40 U.S.P. Units and 80 U.S.P. Units per cc. Each cc. of each strength also contains 0.5% phenol (preservative), 15.0% gelatin, pil adjusted with IICI. This product requires fewer injections per day than aqueous corticotropin preparations to maintain adrenocorticotropic activity. It is solid at or below room temperature; before use, the gel should be liquefied by holding the vial under warm tap water. It should be injected subcutaneously or intramuscularly, never intravenously; a 20 or 21-gauge needle should be used. Injection sites should be alternated, and brief, firm pressure should be applied on the site after each injection.

Properities—This product offers prolonged ACTH activity. It stimulates the adrenals to an increased production of all the adrenocortical hormones. Three types of adrenal hormones are produced in this way: compound F-like hormones