

TX-226, Mesquite Livestock Commission Co., Mesquite, Tex., Jan. 21, 1959.

TX-235, Havard's Horse Sale, Nacogdoches, Tex., Feb. 7, 1967.

TX-239, Palestine Commission Company, Palestine, Tex., June 5, 1967.

TX-260, Sonora Livestock Exchange Company, Sonora, Tex., Sept. 15, 1965.

Notice or other public procedure has not preceded promulgation of the foregoing rule. There is no legal justification for not promptly deposing a stockyard which is no longer within the definition of that term contained in the Act.

The foregoing is in the nature of a rule relieving a restriction and may be made effective in less than 30 days after publication in the FEDERAL REGISTER. This notice shall become effective upon publication in the FEDERAL REGISTER (2-19-72).

(42 Stat. 159, as amended and supplemented; 7 U.S.C. 181 et seq.)

Done at Washington, D.C., this 10th day of February 1972.

EDWARD L. THOMPSON,
Acting Chief, Registrations,
Bonds, and Reports Branch,
Livestock Marketing Division.

[FR Doc.72-2529 Filed 2-18-72;8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[DESI 2354]

COMBINATION DRUG CONTAINING PHENOBARBITAL, ACETAMINOPHEN, PHENACETIN, ATROPINE SULFATE, SCOPOLAMINE HYDROBROMIDE, AND HYOSCYAMINE HYDROBROMIDE

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has evaluated a report received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following drug:

Hasamal tablets containing phenobarbital, acetaminophen, phenacetin, atropine sulfate, scopolamine hydrobromide, and hyoscyamine hydrobromide; Charles C. Haskell Division, Arnar-Stone Laboratories, Inc., 601 East Kensington Road, Mount Prospect, Ill. 60056 (NDA 2-354).

Such drugs are regarded as new drugs (21 U.S.C. 321(p)). The effectiveness classification and marketing status are described below.

A. Effectiveness classification. The Food and Drug Administration has considered the Academy's report, as well as other available evidence, and concludes that the drug:

1. Is possibly effective for relief of pain in headache or toothache, and for symptomatic relief of primary dysmenorrhea.

2. Lacks substantial evidence of effectiveness as a fixed combination for relief of fever.

3. Lacks substantial evidence of effectiveness for relief of cough associated with upper respiratory infection.

B. Marketing status. 1. Within 60 days of the date of publication of this announcement in the FEDERAL REGISTER, the holder of any previously approved new-drug application for which the drug is classified in paragraph A above as lacking substantial evidence of effectiveness is requested to submit a supplement to his application, as needed, to provide for revised labeling which deletes those indications for which substantial evidence of effectiveness is lacking. Such a supplement should be submitted under the provisions of § 130.9 (d) and (e) of the new-drug regulations (21 CFR 130.9 (d) and (e)) which permit certain changes to be put into effect at the earliest possible time, and the revised labeling should be put into use within the 60-day period. Failure to do so may result in a proposal to withdraw approval of the new-drug application.

2. If any such preparation is on the market without an approved new-drug application, its labeling should be revised if it includes those claims for which substantial evidence of effectiveness is lacking as described in paragraph A above. Failure to delete such indications and put the revised labeling into use within 60 days after the date of publication hereof in the FEDERAL REGISTER may cause the drug to be subject to regulatory proceedings.

3. The notice "Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study," published in the FEDERAL REGISTER July 14, 1970 (35 F.R. 11273), (f) the marketing status of a drug labeled with those indications for which it is regarded as possibly effective.

A copy of the Academy's report has been furnished to the firm referred to above. Communications forwarded in response to this announcement should be identified with the reference number DESI 2354, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20852:

Supplements (identify with NDA number):
Office of Scientific Evaluation (BD-100),
Bureau of Drugs.

Original new-drug applications: Office of
Scientific Evaluation (BD-100), Bureau of
Drugs.

Requests for the Academy's report: Drug
Efficacy Study Information Control (BD-
67), Bureau of Drugs.

All other communications regarding this
announcement: Drug Efficacy Study Imple-
mentation Project Office (BD-60), Bureau
of Drugs.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-53, as amended; 21 U.S.C. 352, 355) and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: January 27, 1972.

R. E. DUGGAN,
Acting Associate Commissioner
for Compliance.

[FR Doc.72-2550 Filed 2-18-72;8:45 am]

[DESI 7110; Docket No. FDC-D-291; NDA 7-110, etc.]

CORTISONE; DEXAMETHASONE; HYDROCORTISONE; METHYLPREDNISOLONE; PREDNISOLONE; AND TRIAMCINOLONE FOR PARENTERAL USE

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has evaluated reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following glucocorticoid drugs:

1. Aristocort Forte Suspension, containing triamcinolone diacetate; Lederle Laboratories, Division American Cyanamid Co., Pearl River, N.Y. 10965 (NDA 12-802).

2. Aristocort Intralesional Suspension, containing triamcinolone diacetate; Lederle Laboratories (NDA 11-685).

3. Cortef Acetate Sterile Injectable Suspension, containing hydrocortisone acetate; The Upjohn Co., 7171 Portage Road, Kalamazoo, Michigan 49002 (NDA 9-378).

4. Cortef Sterile Aqueous Suspension, containing hydrocortisone; The Upjohn Co. (NDA 9-864).

5. Cortef Sterile Solution, containing hydrocortisone; The Upjohn Co. (NDA 9-379).

6. Cortiphate Injection, containing hydrocortisone sodium phosphate; Travenol Laboratories, Inc., Division of Baxter Laboratories, Inc., 6301 Lincoln Avenue, Morton Grove, Illinois 60053 (NDA 12-784).

7. Cortisone Acetate Aqueous Suspension; Vitamix Pharmaceuticals, Inc., 2900 North 17th Street, Philadelphia, Pennsylvania 19132 (NDA 10-603).

8. Cortisone Acetate Sterile Aqueous Suspension; The Upjohn Co. (NDA 8-126).

9. Cortone Acetate Saline Suspension, containing cortisone acetate; Merck, Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486 (NDA 7-110).

10. Cortril Aqueous Suspension, containing hydrocortisone acetate; marketed by Chas. Pfizer & Co., Inc., 235 East 42d Street, New York, New York 10017 (NDA 9-164).

11. Cortril Soluble Parenteral, containing hydrocortisone sodium succinate; Chas. Pfizer & Co. (NDA 10-291).

12. Decadron Phosphate Injection, containing dexamethasone sodium phosphate; Merck, Sharp & Dohme (NDA 12-071).

13. Deltacortril Aqueous Suspension, containing prednisolone acetate; Chas. Pfizer & Co. (NDA 11-158).

14. Depo-Medrol Aqueous Suspension, containing methylprednisolone acetate; The Upjohn Co. (NDA 11-757).

15. Hy-Cor Acetate Aqueous Suspension, containing hydrocortisone acetate; Gold Leaf Pharmacal Co., subsidiary of Ormont Drug & Chemical Co., Inc., 223 South Dean Street, Englewood, N.J. 07631 (NDA 9-786).

16. Hydeltasol Injection, containing prednisolone sodium phosphate; Merck, Sharp & Dohme (NDA 11-583).

17. Hydeltro-T.B.A. Suspension, containing prednisolone butylacetate; Merck, Sharp & Dohme (NDA 10-562).

18. Hydrocortisone Acetate Aqueous Suspension; Maurry Biological Co., Inc., 6109 South Western Avenue, Los Angeles, California 90047 (NDA 9-637).

19. Hydrocortisone Acetate Suspension; Philadelphia Laboratories, Inc., 9815 Roosevelt Boulevard, Philadelphia, Pa. 19114 (NDA 10-058).

20. Hydrocortisone Acetate Suspension; Vitamix Pharmaceuticals, Inc. (NDA 10-650).

21. Hydrocortone Acetate Saline Suspension, containing hydrocortisone acetate; Merck, Sharp & Dohme (NDA 8-228).

22. Hydrocortone Phosphate Injection, containing hydrocortisone sodium phosphate; Merck, Sharp & Dohme (NDA 12-052).

23. Hydrocortone-T.B.A. Suspension, containing hydrocortisone butylacetate; Merck, Sharp & Dohme (NDA 9-465).

24. Kenalog Parenteral Aqueous Suspension, containing triamcinolone acetate; E. R. Squibb & Sons, Inc., Georges Road, New Brunswick, New Jersey 08903 (NDA 12-041).

25. Meticortelone Aqueous Suspension, containing prednisolone acetate; Schering Corp., 60 Orange Street, Bloomfield, N.J. 07003 (NDA 10-255).

26. Meticortelone Soluble, containing prednisolone sodium succinate; Schering Corp. (NDA 11-061).

27. Prednisolone Acetate Suspension; Philadelphia Laboratories, Inc. (NDA 11-896).

28. Solu-Cortef Mix-O-Vial, containing hydrocortisone sodium succinate; The Upjohn Co. (NDA 9-866).

29. Solu-Medrol Mix-O-Vial, containing methylprednisolone sodium succinate; The Upjohn Co. (NDA 11-856).

30. Sterane Aqueous Suspension, containing prednisolone acetate; Chas. Pfizer and Co., Inc. (NDA 11-446).

The drugs are regarded as new drugs (21 U.S.C. 321(p)). Supplemental new-drug applications are required to revise the labeling in and to update previously approved applications providing for such drugs. A new-drug application is required from any person marketing such drugs without approval.

The Food and Drug Administration is prepared to approve abbreviated new-drug applications and abbreviated supplements to previously approved new-drug applications under conditions described in this announcement.

A. Effectiveness classification. The Food and Drug Administration has considered the Academy's reports, as well as other available evidence, and concludes that:

1. These preparations for parenteral use are effective or probably effective by the appropriate route of administration for the indications listed in the "Indications" section of this announcement. The probably effective indications are those relating to use in angioedema, urticaria, diffuse interstitial pulmonary

fibrosis (Hamman-Rich Syndrome), intractable sprue, severe trichinosis, dental postoperative inflammatory reactions, ganglia, rectal administration in ulcerative colitis, and use in anaphylaxis.

2. These preparations lack substantial evidence of effectiveness for their recommended use in gout; chronic gouty arthritis; chronic bursitis, synovitis; myositis; fibrositis; plantar fasciitis; intermittent hydrarthrosis; collagen diseases; inflammatory or allergic dermatoses; various other dermatoses; nummular eczema and dermatitis; insect bites or reactions to insect bites; allergy; respiratory allergies; various eye disorders; gastrointestinal diseases; malignant diseases; certain metastatic carcinomas; secondary glaucoma; as rapid diagnostic agents to distinguish between adrenocortical hyperplasia and tumor; osteochondritis; whiplash injuries; hyperextension neck injury; acute torticollis; muscle trauma (avulsion, contusion, hemorrhage); various strains and sprains; lumbago; coccydynia; tensor fascia lata syndrome; hallux rigidus and limitus; trigger points (localized painful areas in muscles); exostosis; calcaneal spur; rheumatoid nodules; neurofibroma; radiculitis; acute dermatoses; surgical infections; retinitis centralis; Rh incompatibilities; "incurable diseases"; sebaceous cyst; acne; alopecia totalis; and pruritis ani.

3. Except as noted above these preparations are possibly effective for their other labeled indications.

B. Form of drug. These glucocorticoid preparations are in aqueous solution or suspension, or sterile powder form suitable for parenteral administration.

C. Labeling conditions. 1. The label bears the statement, "Caution: Federal law prohibits dispensing without prescription."

2. The drug is labeled to comply with all requirements of the Act and regulations promulgated thereunder, and those parts of its labeling indicated below are substantially as follows: (Optional additional information, applicable to the drug, may be proposed under other appropriate paragraph headings and should follow the information set forth below).

DESCRIPTION

(Descriptive information to be included by the manufacturer or distributor should be confined to an appropriate description of the physical and chemical properties of the drug and the formulation.)

ACTIONS

Naturally occurring glucocorticoids (hydrocortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS

A. When oral therapy is not feasible and the strength, dosage form, and route of administration of the drug reasonably lend the preparation to the treatment of the condition, those products labeled for intravenous or intramuscular use are indicated as follows:

1. Endocrine disorders.

Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is of particular importance).

Acute adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; mineralocorticoid supplementation may be necessary, particularly when synthetic analogs are used).

Preoperatively and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful.

Shock unresponsive to conventional therapy if adrenocortical insufficiency exists or is suspected.

Congenital adrenal hyperplasia.
Nonsuppurative thyroiditis.

2. **Rheumatic disorders.** As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:

Post-traumatic osteoarthritis.
Synovitis of osteoarthritis.
Rheumatoid arthritis.
Acute and subacute bursitis.
Epicondylitis.
Acute nonspecific tenosynovitis.
Acute gouty arthritis.
Psoriatic arthritis.
Ankylosing spondylitis.
Juvenile rheumatoid arthritis.

3. **Collagen diseases.** During an exacerbation or as maintenance therapy in selected cases of:

Systemic lupus erythematosus.
Acute rheumatic carditis.

4. Dermatologic diseases. Pemphigus.

Severe erythema multiforme (Stevens-Johnson syndrome).
Exfoliative dermatitis.
Bullous dermatitis herpetiformis.
Severe seborrheic dermatitis.
Severe psoriasis.

5. **Allergic states.** Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in:

Bronchial asthma.
Contact dermatitis.
Atopic dermatitis.
Serum sickness.
Seasonal or perennial allergic rhinitis.
Drug hypersensitivity reactions.
Urticarial transfusion reactions.
Acute noninfectious laryngeal edema (epinephrine is the drug of first choice).

6. **Ophthalmic diseases.** Severe acute and chronic allergic and inflammatory processes involving the eye, such as:

Herpes zoster ophthalmicus.
Iritis, iridocyclitis.
Chorioretinitis.
Diffuse posterior uveitis and choroiditis.
Optic neuritis.
Sympathetic ophthalmia.
Anterior segment inflammation.

7. **Gastrointestinal diseases.** To tide the patient over a critical period of disease in:

Ulcerative colitis—(Systemic therapy).
Regional enteritis—(Systemic therapy).

8. Respiratory diseases.

Symptomatic sarcoidosis.
Berylliosis.
Fulminating or disseminated pulmonary tuberculosis when concurrently accompanied by appropriate antituberculous chemotherapy.
Aspiration pneumonitis.

9. Hematologic disorders.

Acquired (autoimmune) hemolytic anemia. Idiopathic thrombocytopenic purpura in adults (I.V. only; I.M. administration is contraindicated).

10. *Neoplastic diseases.* For palliative management of:

Leukemias and lymphomas in adults. Acute leukemia of childhood.

11. *Edematous state.* To induce diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

12. *Miscellaneous.* Tuberculous meningitis with subarachnoid block or impending block when concurrently accompanied by appropriate antituberculous chemotherapy.

In addition to the above indications, those preparations containing "cortisone, hydrocortisone prednisolone, or methylprednisolone" are indicated for systemic dermatomyositis (polymyositis). Those containing "dexamethasone" are indicated for diagnostic testing of adrenocortical hyperfunction.

All of these drugs may also be useful in the following conditions:

To control severe or incapacitating allergic conditions intractable to adequate trials of convention treatment in angioedema and urticaria and as an adjunct to epinephrine in anaphylaxis; as an enema or drip in selected cases to tide the patient over a critical period of disease in ulcerative colitis, to tide the patient over in a critical period of intractable sprue; in diffuse interstitial pulmonary fibrosis (Hamman-Rich Syndrome); severe trichinosis; and to control dental postoperative inflammatory reactions.

B. When the strength and dosage form of the drug lend the preparation to the treatment of the condition, those products labeled for "intra-articular or soft tissue administration" are indicated:

As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:

Synovitis of osteoarthritis.

Rheumatoid arthritis.

Acute and subacute bursitis.

Acute gouty arthritis.

Epicondylitis.

Acute nonspecific tenosynovitis.

Posttraumatic osteoarthritis.

C. When the strength and dosage form of the drug lend the preparation to the treatment of the condition, those products labeled for "intralesional" administration are indicated for:

Keloids.

Localized hypertrophic, infiltrated, inflammatory lesions of: lichen planus, psoriatic plaques, granuloma annulare and lichen simplex chronicus (neurodermatitis).

Discoid lupus erythematosus.

Necrobiosis lipoidica diabetorum.

Alopecia areata.

They may also be useful in cystic tumors of an aponeurosis or tendon (ganglia).

CONTRAINDICATIONS

Systemic fungal infections.

WARNINGS

In patients on corticosteroid therapy subjected to any unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic

nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Usage in pregnancy. Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers, or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Average and large doses of cortisone or hydrocortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

While on Corticosteroid Therapy Patients Should Not Be Vaccinated Against Smallpox. Other Immunization Procedures Should Not Be Undertaken in Patients Who Are on Corticosteroids, Especially in High Doses, Because of Possible Hazards of Neurological Complications and Lack of Antibody Response.

The use of (name of drug) in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Because rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.

PRECAUTIONS

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstated. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex for fear of corneal perforation.

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction must be gradual.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection, also in diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully followed.

The following additional precautions apply for parenteral corticosteroids. Intra-articular injection of a corticosteroid may produce systemic as well as local effects.

Appropriate examination of any joint fluid present is necessary to exclude a septic process.

A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.

Local injection of a steroid into a previously infected joint is to be avoided.

Corticosteroids should not be injected into unstable joints.

The slower rate of absorption by intramuscular administration should be recognized.

ADVERSE REACTIONS

Fluid and electrolyte disturbances:

Sodium retention.

Fluid retention.

Congestive heart failure in susceptible patients.

Potassium loss.

Hypokalemic alkalosis.

Hypertension.

Musculoskeletal:

Muscle weakness.

Steroid myopathy.

Loss of muscle mass.

Osteoporosis.

Vertebral compression fractures.

Aseptic necrosis of femoral and humeral heads.

Pathologic fracture of long bones.

Gastrointestinal:

Peptic ulcer with possible subsequent perforation and hemorrhage.

Pancreatitis.

Abdominal distention.

Ulcerative esophagitis.

Dermatologic:

Impaired wound healing.

Thin fragile skin.

Petechiae and ecchymoses.

Facial erythema.

Increased sweating.

May suppress reactions to skin tests.

Neurological:

Convulsions.

Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment.

Vertigo.

Headache.

Endocrine:

Menstrual irregularities.

Development of Cushingoid state.

Suppression of growth in children.

Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery, or illness.

Decreased carbohydrate tolerance.

Manifestations of latent diabetes mellitus.

Increased requirements for insulin or oral hypoglycemic agents in diabetics.

Ophthalmic:

Posterior subcapsular cataracts.

Increased intraocular pressure.

Glaucoma.

Exophthalmos.

Metabolic:

Negative nitrogen balance due to protein catabolism.

The following *additional* adverse reactions are related to parenteral corticosteroid therapy:

Rare instances of blindness associated with intralésional therapy around the face and head.

Hyperpigmentation or hypopigmentation.
Subcutaneous and cutaneous atrophy.
Sterile abscess.

Postinjection flare, following intra-articular use).

Charcot-like arthropathy.

DOSAGE AND ADMINISTRATION

The initial dosage of (name) may vary from (insert amount) to (insert amount) mg. per day depending on the specific disease entity being treated. In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. Usually the parenteral dosage ranges are one-third to one-half the oral dose given every 12 hours. However, in certain overwhelming, acute, life-threatening situations, administration in dosages exceeding the usual dosages may be justified and may be in multiples of the oral dosages.

The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response (name) should be discontinued and the patient transferred to other appropriate sponse (name) should be discontinued and therapy. *It Should Be Emphasized That Dosage Requirements Are Variable and Must Be Individualized on the Basis of the Disease Under Treatment and the Response of the Patient.* After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small increments at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of (name) for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

Usual initial parenteral corticosteroid dosages:

	Milligrams per day
Cortisone	20-300
Dexamethasone	0.50-9.0
Hydrocortisone	15-240
Methylprednisolone	3-48
Prednisolone	4-60
Triamcinolone	3-48

D. Marketing status. Marketing of such drugs may be continued under the conditions described in the notice entitled "Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study," published in the FEDERAL REGISTER July 14, 1970 (35 F.R. 11273), as follows:

1. For holders of "deemed approved" new-drug applications (i.e., an application which became effective on the basis of safety prior to October 10, 1962), the submission of a supplement for revised labeling, an abbreviated supplement for updating information, and adequate data to show the biologic availability of the drug in the formulation which is marketed as described in paragraphs (a) (1) (i), (ii), and (iii) of the notice of July 14,

1970. Biologic availability data for a drug administered by the intravenous route is not required.

2. For any person who does not hold an approved or effective new-drug application, the submission of an abbreviated new-drug application, to include adequate data to assure the biologic availability of the drug in the formulation which is or is intended to be marketed, as described in paragraph (a) (3) (ii) of that notice. Biologic availability data for a drug administered by the intravenous route is not required.

3. For any distributor of the drug, the use of labeling in accord with this announcement for any such drug shipped within the jurisdiction of the Act as described in paragraph (b) of that notice.

4. For indications for which the drug has been classified as probably effective (included in the "Indications" section above) and possibly effective (not included in the "Indications" section above), continued use as described in paragraphs (c), (d), (e), and (f) of that notice.

E. Opportunity for a hearing. 1. The Commissioner of Food and Drugs proposes to issue an order under the provisions of section 505(e) of the Federal Food, Drug, and Cosmetic Act withdrawing approval of all new-drug applications and all amendments and supplements thereto providing for the indications for which substantial evidence of effectiveness is lacking as described in paragraph A.2 of this announcement. An order withdrawing approval of the applications will not issue if such applications are supplemented, in accord with this notice, to delete such indications. Any related drug for human use, not the subject of an approved new-drug application, offered for the indications for which substantial evidence of effectiveness is lacking may be affected by this action.

2. In accordance with the provisions of section 505 of the Act (21 U.S.C. 355), and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner will give the holders of any such applications, and any interested person who would be adversely affected by such an order, an opportunity for a hearing to show why such indications should not be deleted from labeling. A request for a hearing must be filed within 30 days after the date of publication of this notice in the FEDERAL REGISTER.

3. A request for a hearing may not rest upon mere allegations or denials but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing, together with a well-organized and full factual analysis of the clinical and other investigational data that the objector is prepared to prove in a hearing. Any data submitted in response to this notice must be previously unsubmitted and include data from adequate and well-controlled clinical investigations (identified for ready review) as described in section 130.12(a)(5) of the regulations published in the FEDERAL REGISTER of May 8, 1970 (35 F.R. 7250). Carefully conducted and documented clinical studies obtained under uncon-

trolled or partially controlled situations are not acceptable as a sole basis for approval of claims of effectiveness, but such studies may be considered on their merits for corroborative support of efficacy and evidence of safety.

4. If a hearing is requested and is justified by the response to this notice, the issues will be defined, a hearing examiner will be named, and he shall issue a written notice of the time and place at which the hearing will commence.

Representatives of the Administration are willing to meet with any interested person who desires to have a conference concerning proposed changes in the labeling set forth herein. Requests for such meetings should be made to the Office of Scientific Evaluation (BD-100), at the address given below, within 30 days after the publication of this notice in the FEDERAL REGISTER.

A copy of the Academy's report has been furnished to each firm referred to above. Communications forwarded in response to this announcement should be identified with the reference number DESI 7110, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20852:

Supplements (Identify with NDA number):
Office of Scientific Evaluation (BD-100),
Bureau of Drugs.

Original abbreviated new-drug applications (Identify as such): Drug Efficacy Study Implementation Project Office (BD-60),
Bureau of Drugs.

Request for hearing (Identify with docket number): Hearing Clerk, Office of General Counsel (GC-1), Room 6-88, Parklawn Building.

Requests for the Academy's report: Drug Efficacy Study Information Control (BD-67),
Bureau of Drugs.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-60), Bureau of Drugs.

Received requests for a hearing may be seen in the office of the Hearing Clerk (address given above) during regular business hours, Monday through Friday.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-53, as amended; 21 U.S.C. 352, 355) and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: February 7, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc. 72-2551 Filed 2-18-72; 8:46 am]

[Docket No. FDC-D-373; NADA No. 5-951V etc.]

DR. MAYFIELD LABORATORIES ET AL. Certain Products Containing Sulfathiazole; Notice of Withdrawal of Approval of New Animal Drug Applications

A notice of opportunity for a hearing was published in the FEDERAL REGISTER