

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
ANDA 85-825

Name: Triamcinolone Acetonide Suspension
40 mg/mL

Sponsor: Carter-Glogau Laboratories, Inc.

Approval Date: November 5, 1981

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 85-825

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 85-825

APPROVAL LETTER

NOV 5 1981

NDA 85-325

Carter-Glogau Laboratories, Inc.
Attention: Samuel M. Fainberg, Ph.D.
5160 West Bethany Home Road
Glendale, AZ 85301

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triamcinolone Acetonide Suspension, 40 mg/ml.

We acknowledge receipt of your communications dated June 4, 1981, August 13 and 20, 1981 enclosing final printed package inserts, and additional control information.

We have completed the review of this abbreviated new drug application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

Any significant change in the conditions outlined in this abbreviated new drug application, requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.3 of the new drug regulations.

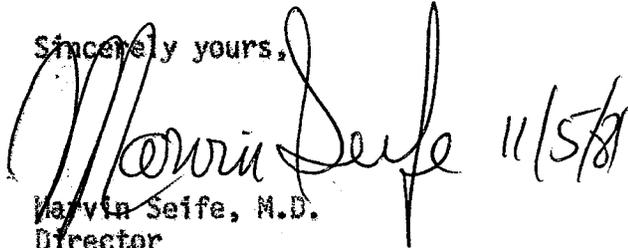
This Administration should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your immediate advertising or promotional campaigns. Please submit both copies and a completed form FD-2253, together with a copy of the Final Printed Labeling, to the Division of Drug Advertising (HFD-170). A copy of Form FD-2253 is enclosed for your convenience.

We call your attention to regulation 21 CFR 310.300(b)(3) which requires that material for any subsequent advertising or promotional campaigns, at the time of their initial use, be submitted to our Division of Drug Advertising (HFD-170) with a completed form FD-2253.

The enclosures summarize the conditions relating to the approval of this application.

Sincerely yours,



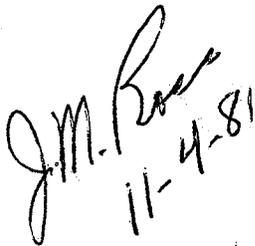
11/5/81

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs

Enclosures:

Conditions of Approval of a New Drug Application
Records & Reports Requirements
Form FD 2253

LOS-DO DUP HFD-531
HFD-313 HFD-616 HFD-5
MSeife/JLMeyer/JMRoss
R/DinitJMeyer/MSeife
ft/cj1/11-4-81
approval



11-4-81

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NOA NUMBER

85-025

DATE APPROVAL LETTER ISSUED

NOV 5 1981

TO:

Press Relations Staff (HFI-40)

FROM:

Bureau of Drugs

Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION

ORIGINAL NDA

TO NDA

ORIGINAL NDA

ORIGINAL ABBREVIATED

SUPPLEMENT TO ANDA

CATEGORY

HUMAN

VETERINARY

TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG

Triamcinolone Acetonide

DOSAGE FORM

suspension

HOW DISPENSED

RX

OTC

ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)

Triamcinolone Acetonide 40 mg./ml

NAME OF APPLICANT (Include City and State)

Carter-Glogau Laboratories, Inc.
5160 West Bethany Home Road
Glendale, AZ. 85301

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

glucocorticoid

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME

J.M. Ross

J.M. Ross

DATE

11-7-81

FORM APPROVED BY

NAME

J.L. Meyer

J.L. Meyer

DATE

11/4/81

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 85-825

LABELING

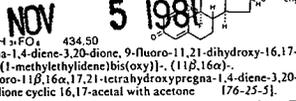
**STERILE TRIAMCINOLONE
ACETONIDE SUSPENSION
40 mg./ml.**

**NOT FOR INTRAVENOUS OR INTRADERMAL USE
FOR INTRAMUSCULAR, INTRA-ARTICULAR
AND SOFT TISSUE USE**

DESCRIPTION: Triamcinolone Acetonide is a white to cream-colored, crystalline powder, having not more than a slight odor.

is practically insoluble in water; very soluble in dehydrated alcohol, in chloroform, and in methanol.

ED



Each ml. of aqueous suspension contains: Triamcinolone Acetonide 40 mg., Sodium Chloride 2 mg., Carboxymethylcellulose Sodium 7.5 mg., Polysorbate 80-0.4 mg., Benzyl Alcohol 0.9% as preservative in Water for Injection q.s. Sodium Hydroxide and/or Hydrochloric Acid used to adjust pH.

CLINICAL PHARMACOLOGY: 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 AND USAGE: *Intramuscular administration.* 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, Triamcinolone Acetonide labeled for intramuscular use is 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 is adrenocortical insufficiency exists or is suspected.

Congenital adrenal hyperplasia.
Nonsuppurative thyroiditis.
Hypercalcemia associated with cancer.

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, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy); acute and subacute bursitis; epicondylitis; acute nonspecific tenosynovitis; acute gouty arthritis; psoriatic arthritis; ankylosing spondylitis.

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; mycosis fungoides.

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; allergic conjunctivitis; allergic corneal marginal ulcers.

7. *Gastrointestinal diseases:* To tide the patient over a critical period of the disease in: Ulcerative colitis (systemic therapy); regional enteritis (systemic therapy).

8. *Respiratory diseases:* Symptomatic sarcoidosis; berylliosis; fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy; Löeffler's syndrome not manageable by other means; aspiration pneumonitis.

9. *Hematologic disorders:* Acquired (autoimmune) hemolytic anemia; idiopathic thrombocytopenic purpura in adults (I.V. only; I.M. administration is contra-indicated); secondary thrombocytopenia in adults; erythroblastopenia (RBC anemia); congenital (erythroid) hypoplastic anemia.

10. *Neoplastic diseases:* For palliative management of: Leukemias and lymphomas in adults; acute leukemia of childhood.

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

12. *Nervous system:* Acute exacerbations of multiple sclerosis.

13. *Miscellaneous:* Tuberculous meningitis with subarachnoid block for impending block when used concurrently with appropriate antituberculous chemotherapy; trichinosis with neurologic or myocardial involvement.

Intra-articular or soft tissue administration. When the strength and dosage form of the drug in the preparation to the treatment of the condition, the 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; post-traumatic osteoarthritis.

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 Triamcinolone Acetonide 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.

Although controlled clinical trials have shown corti-

corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis they do not show that they affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect (See DOSAGE AND ADMINISTRATION Section).

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

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: Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment; convulsions; 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 intralesional therapy around the face and head; hyperpigmentation and hypopigmentation; subcutaneous and cutaneous atrophy; sterile abscess; postinjection flare, (following intra-articular use); charcot-like arthropathy.

DRUG ABUSE AND DEPENDENCE:
(See WARNINGS Section).

OVERDOSAGE:
(See ADVERSE REACTIONS Section).

DOSAGE AND ADMINISTRATION: The initial dosage of Triamcinolone Acetonide Suspension may vary from 2.5 to 60 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 Triamcinolone Acetonide Suspension should be discontinued and the patient transferred to other appropriate 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 Triamcinolone Acetonide Suspension 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.

Triamcinolone Acetonide Suspension 40 mg. per ml. full-strength suspension may be employed. If preferred, the suspension may be diluted with normal saline or water. The diluent may also be prepared by mixing equal parts of normal saline and 1% procaine hydrochloride or other similar local anesthetic. The use of diluents containing preservatives such as methylparaben, propylparaben, phenol, etc. must be avoided as these preparations tend to cause flocculation of the steroid. These dilutions retain full potency for at least one week. Topical ethyl chloride spray may be used locally prior to injection.

INTRAMUSCULAR: Although Triamcinolone Acetonide Suspension may be administered intramuscularly for initial therapy, most physicians prefer to adjust the dose orally until adequate control is attained. Intramuscular administration provides a sustained or depot action which can be used to supplement or replace initial oral therapy. With intramuscular therapy, greater supervision of the amount of steroid used is made possible in the patient who is inconsistent in following an oral dosage schedule. In maintenance therapy, the patient-to-patient response is not uniform and, therefore, the dose must be individualized for optimal control.

Although Triamcinolone Acetonide may possess greater anti-inflammatory potency than many glucocorticoids, this is only dose-related since side effects, such as osteoporosis, peptic ulcer, etc. related to glucocorticoid activity, have not been diminished.

The average dose is 40 mg. (1 ml.) administered intramuscularly once a week. Intraglutally is the preferred route of administration.

In general, a single parenteral dose 4 to 7 times the oral daily dose may be expected to control the patient from 4 to 7 days up to 3 or 4 weeks. Dosage should be adjusted to the point where adequate but not necessarily complete relief of symptoms is obtained.

In the treatment of acute exacerbations of multiple sclerosis daily doses of 200 mg. of prednisolone for a week followed by 80 mg. every other day or 4-8 mg. dexamethasone every other day for 1 month have been shown to be effective (4 mg. of Triamcinolone are equivalent to 5 mg. of prednisolone and 0.75 mg. of dexamethasone).

INTRA-ARTICULAR AND INTRASYNOVIAL: The usual dose varies from 2.5 to 40 mg. The average for the knee, for example, is 25 mg. The duration of effect varies from one week to 2 months. However, acutely inflamed joints may require more frequent injections.

A specific dose depends largely on the size of the joint. Strict surgical asepsis is mandatory. The physician should be familiar with anatomical relationships as described in standard books. Triamcinolone Acetonide Suspension may be used in any accessible joint except the intervertebrals. In general, intrasynovial therapy is suggested under the following circumstances:

1. When systemic steroid therapy is contraindicated because of side effects such as peptic ulcer.
2. When it is desirable to secure relief in one or two specific joints.
3. When good systemic maintenance fails to control flare-ups in a few joints and it is desirable to secure relief without increasing oral therapy.

Such treatment should not be considered to constitute a cure; for although this method will ameliorate the joint symptoms, it does not preclude the need for the conventional measures usually employed.

It is suggested that infiltration of the soft tissue by local anesthetic precede intra-articular injection. A 24-gauge or larger needle on a dry syringe may be inserted into the joint and excess fluid aspirated. Accidental injection into soft tissue decreases the local effectiveness and, by increasing rate of absorption, may produce systemic effects. For the first few hours following injection, there may be local discomfort in the joint but this is usually followed rapidly by effective relief of pain and improvement in local function.

HOW SUPPLIED: Multiple dose vials of 5 ml. containing Triamcinolone Acetonide 40 mg. per ml.

STORE AT ROOM TEMPERATURE.
AVOID FREEZING.

CAUTION: Federal law prohibits dispensing without prescription.

Literature Revised May 1981

Product No. 0204-05

Manufactured by
CARTER-GLOGAU LABORATORIES, INC.
Glendale, Arizona 85301

Labeling: Orig
NDA No: 85-825 Bo. 1-14-80
Reviewed by: JMK

11-481

APPROVED

NDC 0381-0204-05 Multi-dose
TRIAMCINOLONE ACETONIDE SUSPENSION
40 mg. per ml.
NOT FOR INTRAVENOUS OR INTRADERMAL USE
Each ml. contains: Triamcinolone Acetonide 40 mg., Sodium Carboxymethylcellulose 7.5 mg.,
Polyorbate 80 - 0.4 mg., Sodium Chloride 2 mg., Benzyl Alcohol 0.5% as preservative in Water
for Injection n.s., Sodium Hydroxide and/or Hydrochloric Acid to adjust pH. SHAKE WELL BE-
FORE USING. STORE AT ROOM TEMPERATURE (59 degrees to 86 degrees F.) AVOID FREEZ-
ING. USUAL DOSE: FOR INTRAMUSCULAR, INTRA-ARTICULAR AND SOFT-TISSUE USE.
See package insert.
CAUTION: Federal law prohibits dispensing without prescription. 377/0204-05

C CARTER-GLOGAU LABORATORIES, INC.
Glendale, Arizona 85301 5 1981

APPROVED

NDC 0381-0204-05 Multi-dose
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C CARTER-GLOGAU LABORATORIES, INC.
Glendale, Arizona 85301

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CAUTION: Federal law prohibits dispensing without prescription. 377/0204-05

C CARTER-GLOGAU LABORATORIES, INC.
Glendale, Arizona 85301 1981

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 85-825

CHEMISTRY REVIEWS

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
3-10-77

NDA Number
85-825
AF Number

Name and Address of Applicant (City and State)
Carter-Glogau Laboratories Division
~~Chromalloy~~ Chromalloy Pharmaceuticals, Inc.
GeIndale., AZ 85301

Original XX
Amendment _____
Supplement _____
Resubmission _____
Correspondance _____
Report _____
Other _____

Purpose of Amendment/Supplement

Date(s) of Submission(s)
May 9, 1977

Pharmacological Category
glucocorticoid

Name of Drug
Tramcinolone Acetonide

Dosage Form(s)
injection

Potency(ies)
40 mg. per ml.

How Dispensed
Rx x x
OTC

Packaging/Sterilization
(b) (4)

Samples
NA

Related IND/NDA/MF
see Squibb Kenalog

Labeling
satisfactory per RBarzilai

Biologic Availability
Deferred for the present

Establishment Inspection
Requested

Components, Composition, Manufacturing and Controls
Satisfactory except for 1 step in ~~max~~ addition of components and stability.
The supplier (b) (4) will be checked thru HFD ~~120~~ HFD 120

Remarks
Request above with DMF for (b) (4)

Conclusion
Rev w/f JTaylor 6-20-77

REVIEWER *JTaylor* DATE

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date

NDA Number
85-825

AF Number

Name and Address of Applicant (City and State)
Carter-Glogau Laboratories Division
Glenadle, AZ 85301

Original _____
Amendment _____
Supplement _____
Resubmission _____
Correspondance _____
Report _____
Other _____

Purpose of Amendment/Supplement

(b) (4) as ~~xxx~~ supplier

Date(s) of Submission(s)
August 16, 1977

Pharmacological Category
glucocorticoid

Name of Drug
Triamcinolone Acetonide Suspension

Dosage Form(s)
injection

Potency(ies)
40 mg. per ml.

How Dispensed
 Rx
 OTC

Packaging/Sterilization
(b) (4)

Samples
na

Related IND/NDA/MF

Labeling

satisfactory per Rbarailai

Biologic Availability

deferred

Establishment Inspection

requested

Components, Composition, Manufacturing and Controls

need additional stability per current guidelines and commitment to submit data

Remarks

See previous review and per above

Conclusion

*Per w/ft
Taylor 11-8-77*

REVIEWER

DATE

CHEMIST'S REVIEW FOR
ABREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Statement Date:

NDA NUMBER: 85-825

NAME AND ADDRESS OF APPLICANT

Carter-Glogau Laboratories Division
Glendale, AZ 85301

ORIGINAL
AMENDMENT x x
SUPPLEMENT
RESUBMISSION
CORRESPONDENCE
REPORT
OTHER

DATE(s) of SUBMISSION
May 31, 1978

PURPOSE OF AMENDMENT/SUPPLEMENT

PHARMACOLOGICAL CATEGORY

glucocorticoid

NAME OF DRUG

Triamcinolone Acetonide

HOW DISPENSED

RX^x _____ OTC _____

DOSAGE FORM(S)

injection

POTENCY (IES)

40 mg. per ml.

RELATED IND/NDA/DMF

STERILIZATION

(b) (4)

SAMPLES

examined and appear satisfactory

LABELING

satisfactory previously rBarzilai

BIOLOGIC AVAILABILITY

deferred

ESTABLISHMENT INSPECTION

satisfactory per HFD 322

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS

need additional data re particle size and polymorphism.

PACKAGING

(b) (4)

STABILITY

Protocol:

satisfactory

Exp. Date:

2 yr permitted pending development of three lot data

REMARKS AND
CONCLUSION:

Rev w/f Per letter ~~no~~ of issue



3. NAME AND ADDRESS OF APPLICANT (City and State) Carter-Glogau Laboratories, Inc. Glendale, AZ		4. AF NUMBER 85-825 DESI 7110	
6. NAME OF DRUG		7. NONPROPRIETARY NAME Triamcinolone Acetonide	
8. SUPPLEMENT(S) PROVIDES FOR: Amendments 9-6-79, 9-20-79, 10-29-79, 3-18-81, 4/13/81		5. SUPPLEMENT(S) NUMBER(S) DATE(S) 2-19-72	
10. PHARMACOLOGICAL CATEGORY Glucocorticoid		11. HOW DISPENSED <input checked="" type="checkbox"/> RX <input type="checkbox"/> OTC	
13. DOSAGE FORM (S) Injection/Suspension		14. POTENCY (ies) 40 mg./ml.	
15. CHEMICAL NAME AND STRUCTURE		12. RELATED IND/NDA/DMF(S)	
		16. RECORDS AND REPORTS CURRENT <input type="checkbox"/> YES <input type="checkbox"/> NO REVIEWED <input type="checkbox"/> YES <input type="checkbox"/> NO	
17. COMMENTS Bioavailability is deferred for IV use per FR notice dated 2-19-72 37:3776; bio requirement in notice dated 3-1-77 for parenteral suspensions to be deferred per Dr. Seife since the requirement has not been previously imposed on similar products prior to their approval. See attachment			
18. CONCLUSIONS AND RECOMMENDATIONS Notify firm deficiencies			
19. NAME R.C. Permisohn		REVIEWER SIGNATURE <i>R. Permisohn</i>	
		DATE COMPLETED 5/21/81	
DISTRIBUTION <input type="checkbox"/>		ORIGINAL JACKET <input type="checkbox"/>	
		REVIEWER <input type="checkbox"/>	
		DIVISION FILE <input type="checkbox"/>	

FORM FDH 2265 (7/75)

PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

Following this page, 2 pages withheld in full- (b)(4)

30. Samples are not required since the product is a compendium item.

31. Labeling (4)

Satisfactory per MO/RB. However, name & address of mfg, excluded from insert labeling & only revised labeling for 5 ml. vial provided.

2626E

Enter evaluation or comments for each item. If necessary, continue on 8" x 10 1/2" paper. Key continuation to item by number. Enter "NC" if no change or "NA" if not applicable.		NDA NUMBER 85-825
25. COMPONENTS AND COMPOSITION (6, 7) see attached sheet		
26. XXXXXXXXXXXXXXXXXXXXXXXXXXXX Suppliers of the active ingredient: 1. (b) (4) (DMF No. (b) (4)) U.S.P. material as per DMF. 2. (b) (4)		
27. SYNTHESIS (8c) 3. (b) (4) U.S.P. material as per DMF No. (b) (4) U.S.P. Material as per DMF No. (b) (4)		
28. RAW MATERIAL CONTROLS (8d,e) a. NEW DRUG SUBSTANCE active ingredient is tested as per USP b. OTHER INGREDIENTS excipients are tested as per USP/NF		
29. OTHER FIRM(s) (8f) (b) (4) performs all laboratory tests has submitted Certification Statement		
30. MANUFACTURING AND PROCESSING (8g,h,i,k) manufacturing instructions submitted		
31. CONTAINER (8i) with 5 ml Type I Glass vials (b) (4) Grey (b) (4) Stopper		
32. PACKAGING AND LABELING (8l,m)		
33. LABORATORY CONTROLS (In-Process and Finished Dosage Form) (8n) finished dosage form is tested as per USP		
34. STABILITY (8p) Lot # 78C025- Rm. Temp-5ml vial- 24 mos. data Lot 78J020- " " " - 24 mos. " Lot 78E069- " " " - 24 mos. " Lot # 79A023 - " " " " - 24 mos. " Stability Reporting format will include USP Testing and Resuspension Syringeability Homogeneity Particle Size		
36. SAMPLES AND RESULTS (9) a. VALIDATION not requested b. MARKET PACKAGE		
37. LABELING (4) container labels: Satisfactory(MSeife) package insert: " "		
38. ESTABLISHMENT INSPECTION Carter Glogau Labs. "All incomppliance as per (b) (4) HFD 322 memo 5/28/81		
39. RECALLS		

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 85-825

MEDICAL REVIEW

REVIEW OF ANDA'S

DATE COMPLETED: 6-13-77

ANDA #: 85-825 40 mg/ml.
(b) (4)

CO. NAME: Carter-Glogau

NAME OF DRUG: Triamcinolone Hexacetonide Suspension USP - Not for intravenous use.

DATE OF SUBMISSION: 5-9-77

TYPE OF SUBMISSION: ANDA

CLINICAL EVALUATION:

1. Review of Studies:

EIAR - for review by assigned chemist.
Bio studies - deferred.

2. Review of Labeling:

a) Container labels: Acceptable FPL

b) Package insert: Acceptable FPL proposing the (b) (4) for (b) (4) and "intraarticular" routes of administration and the 40 mg/ml. potency to add "soft tissue use" and excluding the "intradermal use".

CONCLUSION: Acceptable FPL.

RECOMMENDATIONS:

1. Needs chemists review.
2. Acceptable FPL.


R. Barzilai, M.D.

cc:dup
REB/wlb/6-15-77

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 85-825

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



CHROMALLOY PHARMACEUTICALS, INC.

A SUBSIDIARY OF CHROMALLOY AMERICAN CORPORATION

CARTER-GLOGAU LABORATORIES DIVISION

May 9, 1977

ABBREVIATED
NEW DRUG APPLICATION
85-825

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education, and Welfare
Public Health Service
Food and Drug Administration
Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml.

Dear Dr. Seife:

Enclosed please find, in triplicate, our abbreviated New Drug Application for Triamcinolone Acetonide Suspension, 40 mg/ml.

Sincerely yours,

CARTER-GLOGAU LABORATORIES DIVISION
CHROMALLOY PHARMACEUTICALS, INC.

Samuel M. Fainberg, Ph.D.
Director
Technical and Regulatory Affairs

SMF/jcw
encl



GENERAL OFFICES:
5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301
TELEPHONE (602) 939-7565 • TELEX 66-8304 (M-C LABS)

NEW DRUG APPLICATION (DRUGS FOR HUMAN USE)
(Title 21, Code of Federal Regulations, § 130.4)

Name of applicant CARTER-GLOGAU LABORATORIES DIVISION, CHROMALLOY PHARMACEUTICALS, INC.

Address 5160 W. BETHANY HOME ROAD, GLENDALE, AZ 85301

Date May 9, 1977

Name of new drug TRIAMCINOLONE ACETONIDE SUSPENSION USP 40 MG/ML.

- | | |
|--|---|
| <input type="checkbox"/> Original application (regulation § 130.4). | <input type="checkbox"/> Amendment to abbreviated, unapproved application (regulation § 130.7). |
| <input type="checkbox"/> Amendment to original, unapproved application (regulation § 130.7). | <input type="checkbox"/> Supplement to an approved application (regulation § 130.9). |
| <input checked="" type="checkbox"/> Abbreviated application (regulation § 130.4(f)). | <input type="checkbox"/> Amendment to supplement to an approved application. |

The undersigned submits this application for a new drug pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act. It is understood that when this application is approved, the labeling and advertising for the drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application; and if the article is a prescription drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the drug will contain the same information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant warnings, hazards, contraindications, side effects, and precautions, as that contained in the labeling which is part of this application in accord with § 1.106(b) (21 CFR 1.106(b)). It is understood that all representations in this application apply to the drug produced until an approved supplement to the application provides for a change or the change is made in conformance with other provisions of § 130.9 of the new-drug regulations.

Attached hereto, submitted in the form described in § 130.4(e) of the new-drug regulations, and constituting a part of this application are the following:

1. Table of contents. The table of contents should specify the volume number and the page number in which the complete and detailed item is located and the volume number and the page number in which the summary of that item is located (if any).

2. Summary. A summary demonstrating that the application is well-organized, adequately tabulated, statistically analyzed (where appropriate), and coherent and that it presents a sound basis for the approval requested. The summary should include the following information: (In lieu of the outline described below and the evaluation described in Item 3, an expanded summary and evaluation may be submitted to facilitate the review of this application.)

- a. Chemistry.
 - i. Chemical structural formula or description for any new-drug substance.
 - ii. Relationship to other chemically or pharmacologically related drugs.
 - iii. Description of dosage form and quantitative composition.
- b. Scientific rationale and purpose the drug is to serve.
- c. Reference number of the investigational drug notice(s) under which this drug was investigated and of any notice, new-drug application, or master file of which any contents are being incorporated by reference to support this application.
- d. Preclinical studies. (Present all findings including all adverse experiences which may be interpreted as incidental or not drug-related. Refer to date and page number of the investigational drug notice(s) or the volume and page number of this application where complete data and reports appear.)
 - i. Pharmacology (pharmacodynamics, endocrinology, metabolism, etc.).

ii. Toxicology, and pathology: Acute toxicity studies; subacute and chronic toxicity studies; reproduction and teratology studies; miscellaneous studies.

e. Clinical studies. (All material should refer specifically to each clinical investigator and to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found.)

- i. Special studies not described elsewhere.
- ii. Dose-range studies.
- iii. Controlled clinical studies.
- iv. Other clinical studies (for example, uncontrolled or incompletely controlled studies).
- v. Clinical laboratory studies related to effectiveness.
- vi. Clinical laboratory studies related to safety.
- vii. Summary of literature and unpublished reports available to the applicant.

3. Evaluation of safety and effectiveness. a. Summarize separately the favorable and unfavorable evidence for each claim in the package labeling. Include references to the volume and page number in the application and in any documents incorporated by reference where the complete data and reports may be found.

b. Include tabulation of all side effects or adverse experience, by age, sex, and dosage formulation, whether or not considered to be significant, showing whether administration of the drug was stopped and showing the investigator's name with a reference to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found. Indicate those side effects or adverse experiences considered to be drug-related.

4. Copies of the label and all other labeling to be used for the drug (a total of 12 copies if in final printed form, 4 copies if in draft form):



a. Each label, or other labeling, should be clearly identified to show its position on, or the manner in which it accompanies, the market package.

b. If the drug is to be offered over the counter, labeling on or within the retail package should include adequate directions for use by the layman under all the conditions for which the drug is intended for lay use or is to be prescribed, recommended, or suggested in any labeling or advertising sponsored by or on behalf of the applicant and directed to the layman. If the drug is intended or offered for uses under the professional supervision of a practitioner licensed by law to administer it, the application should also contain labeling that includes adequate information for all such uses, including all the purposes for which the over-the-counter drug is to be advertised to, or represented for use by, physicians.

c. If the drug is limited in its labeling to use under the professional supervision of a practitioner licensed by law to administer it, its labeling should bear information for use under which such practitioners can use the drug for the purposes for which it is intended, including all the purposes for which it is to be advertised or represented, in accord with §1.106(b) (21 CFR 1.106(b)). The application should include any labeling for the drug intended to be made available to the layman.

d. If no established name exists for a new-drug substance, the application shall propose a nonproprietary name for use as the established name for the substance.

e. Typewritten or other draft labeling copy may be submitted for preliminary consideration of an application. An application will not ordinarily be approved prior to the submission of the final printed label and labeling of the drug.

f. No application may be approved if the labeling is false or misleading in any particular.

(When mailing pieces, any other labeling, or advertising copy are devised for promotion of the new drug, samples shall be submitted at the time of initial dissemination of such labeling and at the time of initial placement of any such advertising for a prescription drug (see §130.13 of the new-drug regulations). Approval of a supplemental new-drug application is required prior to use of any promotional claims not covered by the approved application.)

5. A statement as to whether the drug is (or is not) limited in its labeling and by this application to use under the professional supervision of a practitioner licensed by law to administer it.

6. A full list of the articles used as components of the drug. This list should include all substances used in the synthesis, extraction, or other method of preparation of any new-drug substance, and in the preparation of the finished dosage form, regardless of whether they undergo chemical change or are removed in the process. Each substance should be identified by its established name, if any, or complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified.

7. A full statement of the composition of the drug. The statement shall set forth the name and amount of each ingredient, whether active or not, contained in a stated quantity of the drug in the form in which it is to be distributed (for example, amount per tablet or per milliliter) and a batch formula representative of that to be employed for the manufacture of the finished dosage form. All components should be included in the batch formula regardless of whether they appear in the finished product. Any calculated excess of an ingredient over the label declaration should be designated as such and percent excess shown. Reasonable variations may be specified.

8. A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug. Included in this description should be full information with respect to any new-drug substance and to the new-drug dosage form, as follows, in sufficient detail to permit evaluation of the adequacy of the described methods of manufacture, processing, and packing and the described facilities and controls to determine and preserve the identity, strength, quality, and purity of the drug:

a. A description of the physical facilities including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.

b. A description of the qualifications, including educational background and experience, of the technical and professional personnel who are responsible for assuring that the drug has the safety, identity, strength, quality, and purity it purports or is represented to possess, and a statement of their responsibilities.

c. The methods used in the synthesis, extraction, isolation, or purification of any new-drug substance. When the specifications and controls applied to such substance are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperatures, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the substance may be specified.

d. Precautions to assure proper identity, strength, quality, and purity of the raw materials, whether active or not, including the specifications for acceptance and methods of testing for each lot of raw material.

e. Whether or not each lot of raw materials is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.

f. If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new-drug substance or the new-drug dosage form, his statement identifying each person who will perform any part of such operations and designating the part; and a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls in his part of the operation.

g. Method of preparation of the master formula records and individual batch records and manner in which these records are used.

b. The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new drug, including any special precautions observed in the operations.

i. Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

j. Number of individuals checking weight or volume of each individual ingredient entering into each batch of the drug.

k. Whether or not the total weight or volume of each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the formula card and, if so, at what stage and by whom it is done.

l. Precautions to check the actual package yield produced from a batch of the drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in the event of an unexplained discrepancy.

m. Precautions to assure that each lot of the drug is packaged with the proper label and labeling, including provisions for labeling storage and inventory control.

n. The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components. If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

o. An explanation of the exact significance of the batch control numbers used in the manufacturing, processing, packaging, and labeling of the drug, including the control numbers that appear on the label of the finished article. State whether these numbers enable determination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch if its recall is required.

p. A complete description of, and data derived from, studies of the stability of the drug, including information showing the suitability of the analytical methods used. Describe any additional stability studies underway or contemplated. Stability data should be submitted for any new-drug substance, for the finished dosage form of the drug in the container in which it is to be marketed, including any proposed multiple-dose container, and if it is to be put into solution at the time of dispensing, for the solution prepared as directed. State the expiration date(s) that will be used on the label to preserve the identity, strength, quality, and purity of the drug until it is used. (If no expiration date is proposed, the applicant must justify its absence.)

q. Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product.

(An application may be refused unless it includes adequate information showing that the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the drug are adequate to preserve its identity, strength, quality, and purity in conformity with good manufacturing practice and identifies each establishment, showing the location of the plant conducting these operations.)

9. Samples of the drug and articles used as components, as follows: a. The following samples shall be submitted with the application or as soon thereafter as they become available. Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assays:

i. A representative sample or samples of the finished dosage form(s) proposed in the application and employed in the clinical investigations and a representative sample or samples of each new-drug substance, as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

ii. A representative sample or samples of finished market packages of each dosage form of the drug prepared for initial marketing and, if any such sample is not from a commercial-scale production batch, such a sample from a representative commercial-scale production batch; and a representative sample or samples of each new-drug substance as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

iii. A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new-drug substance and other assayed

components of the finished drug: *Provided, however,* That samples of reference standards recognized in the official U.S. Pharmacopeia or The National Formulary need not be submitted unless requested.

b. Additional samples shall be submitted on request.

c. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new-drug application to which it relates.

d. There shall be included a full list of the samples submitted pursuant to Item 9a; a statement of the additional samples that will be submitted as soon as available; and, with respect to each sample submitted, full information with respect to its identity, the origin of any new-drug substance contained therein (including in the case of new-drug substances, a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays. Include for any reference standard a complete description of its preparation and the results of all laboratory tests on it. If the test methods used differed from those described in the application, full details of the methods employed in obtaining the reported results shall be submitted.

e. The requirements of Item 9a may be waived in whole or in part on request of the applicant or otherwise when any such samples are not necessary.

f. If samples of the drug are sent under separate cover, they should be addressed to the attention of the Bureau of Medicine and identified on the outside of the shipping carton with the name of the applicant and the name of the drug as shown on the application.

10. Full reports of preclinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate preclinical tests by all methods reasonably applicable to a determination of the safety and effectiveness of the drug under the conditions of use suggested in the proposed labeling.

b. Detailed reports of the preclinical investigations, including all studies made on laboratory animals, the methods used, and the results obtained, should be clearly set forth. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the underlying data are available for inspection. The animal studies may not be considered adequate unless they give proper attention to the conditions of use recommended in the proposed labeling for the drug such as, for example, whether the drug is for short- or long-term administration or whether it is to be used in infants, children, pregnant women, or women of child-bearing potential.

c. Detailed reports of any pertinent microbiological and *in vitro* studies.

d. Summarize and provide a list of literature references (if available) to all other preclinical information known to the applicant, whether published or unpublished, that is pertinent to an evaluation of the safety or effectiveness of the drug.

11. List of investigators. a. A complete list of all investigators supplied with the drug including the name and post office address of each investigator and, following each name, the volume and page references to the investigator's report(s) in this application and in any documents incorporated by reference, or the explanation of the omission of any reports.

b. The unexplained omission of any reports of investigations made with the new drug by the applicant, or

submitted to him by an investigator, or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources, whether or not it would bias an evaluation of the safety of the drug or its effectiveness in use, may constitute grounds for the refusal or withdrawal of the approval of an application.

12. Full reports of clinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the drug is safe and effective for use as suggested in the labeling.

b. An application may be refused unless it includes substantial evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

c. Reports of all clinical tests sponsored by the applicant or received or otherwise obtained by the applicant should be attached. These reports should include adequate information concerning each subject treated with the drug or employed as a control, including age, sex, conditions treated, dosage, frequency of administration of the drug, results of all relevant clinical observations and laboratory examinations made, full information concerning any other treatment given previously or concurrently, and a full statement of adverse effects and useful results observed, together with an opinion as to whether such effects or results are attributable to the drug under investigation and a statement of where the underlying data are available for inspection. Ordinarily, the reports of clinical studies will not be regarded as adequate unless they include reports from more than one independent, competent investigator who maintains adequate case histories of an adequate number of subjects, designed to record observations and permit evaluation of any and all discernible effects attributable to the drug in each individual treated and comparable records on any individuals employed as controls. An application for a combination drug may be refused unless there is substantial evidence that each ingredient designated as active makes a contribution to the total effect claimed for the drug combination. Except when the disease for which the drug is being tested occurs with such infrequency in the United States as to make testing impractical, some of the investigations should be performed by competent investigators within the United States.

d. Attach as a separate section a completed Form FD-1639, Drug Experience Report (obtainable, with instructions, on request from the Department of HEW, Food and Drug Administration, Bureau of Drugs (BD-200) Rockville, Maryland 20852), for each adverse experience or, if feasible, for each subject or patient experiencing one or more adverse effects, described in Item 12c, whether or not full information is available. Form FD-1639 should be prepared by the applicant if the adverse experience was not reported in such form by the investigator. The Drug Experience Report should be cross-referenced to any narrative description included in Item 12c. In lieu of a FD Form 1639, a computer-generated report may be submitted if equivalent in all elements of information with the identical enumerated sequence of events and methods of completion; all formats proposed for such use will require initial review and approval by the Food and Drug Administration.

e. All information pertinent to an evaluation of the safety and effectiveness of the drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commercial marketing (for example, outside the United States), or reports in the scientific literature, involving the drug that is the subject of the application and related drugs. An adequate summary may be acceptable in lieu of a reprint of a published report which only supports other data submitted. Reprints are not required of reports in designated journals, listed in §130.38 of the new-drug regulations, about related drugs; a bibliography will suffice. Include any evaluation of the safety or effectiveness of the drug that has been made by the applicant's medical department, expert committee, or consultants.

f. If the drug is a combination of previously investigated or marketed drugs, an adequate summary of pre-existing information from preclinical and clinical investigation and experience with its components, including all reports received or otherwise obtained by the applicant suggesting side effects, contraindications, and ineffectiveness in use of such components. Such summary should include an adequate bibliography of publications about the components and may incorporate by reference information concerning such components previously submitted by the applicant to the Food and Drug Administration.

g. The complete composition and/or method of manufacture of the new drug used in each submitted report of investigation should be shown to the extent necessary to establish its identity, strength, quality, and purity if it differs from the description in Item 6, 7, or 8 of the application.

13. If this is a supplemental application, full information on each proposed change concerning any statement made in the approved application.

Observe the provisions of §130.9 of the new-drug regulations concerning supplemental applications.

CARTER-GLOGAU LABORATORIES DIVISION
CHROMALLOY PHARMACEUTICALS, INC.

(Applicant)

Per

(Responsible official or agent)

SAMUEL M. FAINBERG, Ph.D., DIRECTOR,
TECHNICAL AND REGULATORY AFFAIRS

(Indicate authority)

(Warning: A willfully false statement is a criminal offense. U.S.C. Title 18, sec. 1001.)

NOTE: This application must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of and must be countersigned by an authorized attorney, agent, or official residing or maintaining a place of business within the United States.

JUN 7 1977

NDA 85-825

Carter-Glogau Laboratories Division
Chromalloy Pharmaceuticals, Inc.
Attention: Samuel M. Fainberg, Ph.D.
5160 W. Bethany Home Road
Glendale, AZ 85301

Gentlemen:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NAME OF DRUG: Triamcinolone Acetonide Suspension 40 mg/ml

DATE OF APPLICATION: May 9, 1977

DATE OF RECEIPT: May 18, 1977

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the NDA number shown above.

LOS-DO DUP HFD-614, HFD-616
JLMeyer/cjb/6-6-77 ack

JLMeyer 6/6/77

Sincerely yours,

Marvin Seife 6/7/77

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs

TX-225, Mesquite Livestock Commission Co., Mesquite, Tex., Jan. 21, 1951.
TX-225, Edwards House Sale, Kacogdoches, Tex., Feb. 7, 1957.
TX-229, Palestine Commission Company, Palestine, Tex., June 5, 1957.
TX-263, Sonora Livestock Exchange Company, Sonora, Tex., Sept. 15, 1955.

Notice or other public procedure has not preceded promulgation of the foregoing rule. There is no legal justification for not promptly depositing 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, Amnars-Stone Laboratories, Inc., 601 East Kensington Road, Mount Prospect, Ill. 60053 (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 a 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-159),
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 Implementation 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. 1659-53, as amended; 21 U.S.C. 352, 355) and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.1207).

Dated: January 27, 1972.

R. H. DURAN,
*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 12-302).

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 9-364).

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 12-764).

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. 19386 (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 11-159).

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 Pharmaceutical Co., subsidiary of Ormont Drug & Chemical Co., Inc., 222 South Dean Street, Englewood, N.J. 07631 (NDA 9-786).

16. Hydrocortisone Acetate Injection, containing prednisolone sodium phosphate; Merck, Sharp & Dohme (NDA 11-563).

17. Hydrocortisone-T.B.A. Suspension, containing prednisolone butylacetate; Merck, Sharp & Dohme (NDA 10-553).

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

19. Hydrocortisone Acetate Suspension; Philadelphia Laboratories, Inc., 9315 Roosevelt Boulevard, Philadelphia, Pa. 19114 (NDA 10-058).

20. Hydrocortisone Acetate Suspension; Vitamix Pharmaceuticals, Inc. (NDA 10-630).

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

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

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

24. Kenalog Parenteral Aqueous Suspension, containing triamcinolone acetonide; E. R. Squibb & Sons, Inc., Georges Road, New Brunswick, New Jersey 07903 (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 10-896).

28. Solu-Cortef Mix-O-Vial, containing hydrocortisone sodium succinate; The Upjohn Co. (NDA 9-366).

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. The indications listed in the "Indications" section of this announcement probably effective indications are relating to use in angiodema, urticaria, diffuse interstitial pulmonary

fibrosis (Hamman-Rich Syndrome), intractable sprue, severe trichinosis, dental postoperative inflammation, rheumatoid arthritis, 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 limit the preparation to the treatment of the condition, these products labeled for intravenous or intramuscular use are indicated as follows:

1. Endocrine disorders.

Primary or secondary adrenocortical deficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogs are 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.

Rhinitis.

Emphysematous or disseminated pulmonary tuberculosis when concurrently accompanied by appropriate antituberculous chemotherapy.

Aspiration pneumonia.

9. Hemolytic 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 conventional 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 (Hammann-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:

Acute 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

nerve, 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 hypoprothrombemia.

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, peptic ulcerative anastomosis, 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 hives associated with intrathecal therapy around the face and neck.

Hyperpigmentation or hypopigmentation, Subcutaneous and cutaneous atrophy, Sterile abscesses.

Postinjection flare, following intra-articular use).

Charcot-like arthropathy.

DOSEAGE 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 spouse (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	0.50-2.0
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. 11272), 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), (3), 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 insure biologic availability of the drug in the formulation which is or is intended to be marketed, as described in paragraph (b) (3) (ii) of the notice of July 14, 1970, 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 120), 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) (3) of the regulations published in the Federal Register of May 3, 1970 (35 F.R. 7258). 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-63),
Bureau of Drugs.

Request for hearing (Identify with docket number): Hearing Clerk, Office of General Counsel (GC-1), Room 6-26, 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. 1659-53, 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. 5-581V 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

of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and 21 CFR 314.111 (a) (5), demonstrating the effectiveness of the drug(s) for the indication(s) lacking substantial evidence of effectiveness referred to in paragraph A. of this notice.

Notice is given to the holder(s) of the new drug application(s), and to all other interested persons, that the Director of the Bureau of Drugs proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of the new drug application(s) and all amendments and supplements thereto providing for the indication(s) lacking substantial evidence of effectiveness referred to in paragraph A. of this notice on the ground that new information before him with respect to the drug product(s), evaluated together with the evidence available to him at the time of approval of the application(s), shows there is a lack of substantial evidence that the drug product(s) will have all the effects it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling. An order withdrawing approval will not issue with respect to any application(s) supplemented, in accord with this notice, to delete the claim(s) lacking substantial evidence of effectiveness.

In addition to the ground for the proposed withdrawal of approval stated above, this notice of opportunity for hearing encompasses all issues relating to the legal status of the drug products subject to it (including identical, related, or similar drug products as defined in 21 CFR 310.6), e.g., any contention that any such product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act or because it is exempt from part or all of the new drug provisions of the act pursuant to the exemption for products marketed prior to June 25, 1938, contained in section 201(p) of the act, or pursuant to section 107(c) of the Drug Amendments of 1962; or for any other reason.

In accordance with the provisions of section 505 of the act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Parts 310, 314), the applicant(s) and all other persons who manufacture or distribute a drug product which is identical, related, or similar to a drug product named above (21 CFR 310.6), are hereby given an opportunity for a hearing to show why approval of the new drug application(s) providing for the claim(s) involved should not be withdrawn and an opportunity to raise, for administrative determination, all issues relating to the legal status of a drug product named above and all identical, related, or similar drug products.

If an applicant or any person subject to this notice pursuant to 21 CFR 310.6 elects to avail himself of the opportunity for a hearing, he shall file (1) on or before March 31, 1977, a written notice of appearance and request for hearing, and (2) on or before May 2, 1977, the data, information, and analyses on which he

relies to justify a hearing, as specified in 21 CFR 314.200. Any other interested person may also submit comments on this proposal to withdraw approval. The procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, a submission of data, information, and analyses to justify a hearing, other comments, and a grant or denial of hearing, are contained in 21 CFR 314.200.

The failure of an applicant or any other person subject to this notice pursuant to 21 CFR 310.6 to file timely written appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by such person not to avail himself of the opportunity for a hearing concerning the action proposed with respect to such drug product and a waiver of any contentions concerning the legal status of such drug product. Any such drug product labeled for the indication(s) lacking substantial evidence of effectiveness referred to in paragraph A. of this notice may not thereafter lawfully be marketed, and the Food and Drug Administration will initiate appropriate regulatory action to remove such drug products from the market. Any new drug product marketed without an approved NDA is subject to regulatory action at any time.

A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for the hearing that there is no genuine and substantial issue of fact which precludes the withdrawal of approval of the application, or when a request for hearing is not made in the required format or with the required analysis, the Commissioner will enter summary judgment against the person(s) who requests the hearing, making findings and conclusions, denying a hearing.

All submissions pursuant to this notice of opportunity for hearing shall be filed in quintuplicate. Such submissions, except for data and information prohibited from public disclosure pursuant to 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the office of the Hearing Clerk (address given below) during working hours, Monday through Friday.

Communications forwarded in response to this notice should be identified with the reference number DESI 7110, directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Supplements (identify with NDA number): Division of Metabolism and Endocrine Drug Products (HFD-130), Rm. 14B-03, Bureau of Drugs.

Original abbreviated new drug applications (identify as such): Division of Generic Drug Monographs (HFD-530), Bureau of Drugs.

Request for Hearing (identify with Docket number appearing in the heading of this notice): Hearing Clerk, Food and Drug Administration (HFC-20), Rm. 4-65.

Requests for the report of the National Academy of Sciences-National Research Council: Public Records and Document Center (HFC-18), Rm. 4-62.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFD-501), Bureau of Drugs.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-1053, as amended (21 U.S.C. 352, 355)) and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.31) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)).

Dated: February 18, 1977.

J. RICHARD CROUT,
Director, Bureau of Drugs.

[FR Doc.77-6039 Filed 2-28-77; 8:45 am]

[Docket No. 76N-0328; DESI 7110]

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

Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice and Opportunity for Hearing

In a notice (DESI 7110; Docket No. FDC-D-291 (now Docket No. 76N-0328)) published in the FEDERAL REGISTER of February 19, 1972 (37 FR 3775), the Food and Drug Administration (FDA) announced its conclusions that the anti-inflammatory drug products described in section I below are effective or probably effective by the appropriate route of administration for certain indications and possibly effective or lacking substantial evidence of effectiveness for their other labeled indications. The notice also offered an opportunity for a hearing concerning the indications concluded at that time to lack substantial evidence of effectiveness. No data in support of any of the less-than-effective indications were submitted. This notice offers an opportunity for a hearing concerning those indications, and sets forth the conditions for marketing the drug products for the indications for which they are now regarded as effective. Persons who wish to request a hearing may do so on or before March 31, 1977.

All of the products named in the notice of February 19, 1972 and included in section I below are subjects of new drug applications that became effective prior to October 10, 1962. All are formulated and packaged for parenteral administration. Among the indications classified as probably effective in that notice was the indication for rectal use as an enema or drip in ulcerative colitis. None of the products are formulated and packaged especially for rectal administration. In that no data were submitted in support of rectal use of any of these

parenteral products, that indication is one of the indications now being reclassified as lacking substantial evidence of effectiveness.

Three rectally administered corticosteroid products have been approved as both safe and effective since October 9, 1962. All of them are formulated and packaged especially for rectal administration. These products are named and discussed in section II below.

I. Parenteral Corticosteroids Included in the Notice of February 19, 1972.

The notice that follows does not pertain to the indications stated in the February 19, 1972 notice to lack substantial evidence of effectiveness. No person requested a hearing concerning them, and they are no longer allowable in the labeling. Any such product labeled for those indications is subject to regulatory action.

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

2. That part of NDA 8-126 pertaining to Cortisone Acetate Sterile Aqueous Suspension; The Upjohn Co., 7171 Portage Rd., Kalamazoo, MI 49002.

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

4. NDA 9-164; Cortril Aqueous Suspension containing hydrocortisone acetate; Pfizer Laboratories, Division Pfizer, Inc., 235 E. 42d St., New York, NY 10017.

5. NDA 9-378; Cortef Acetate Sterile Injectable Suspension containing hydrocortisone acetate; The Upjohn Co.

6. NDA 9-379; Cortef Sterile Solution containing hydrocortisone; The Upjohn Co.

7. NDA 9-637; Hydrocortisone Acetate Aqueous Suspension; H. E. Maurry Biological Co., Inc., 6109 S. Western Ave., Los Angeles, CA 90047.

8. NDA 9-786; Hy-Cor Acetate Aqueous Suspension containing hydrocortisone acetate; Gold Leaf Pharmacal Co., Inc., 520 S. Dean St., Englewood, NJ 07631.

9. NDA 9-864; Cortef Sterile Aqueous Suspension containing hydrocortisone; The Upjohn Co.

10. NDA 9-866; Solu-Cortef Mix-O-Vial containing hydrocortisone sodium succinate; The Upjohn Co.

11. NDA 10-058; Hydrocortisone Acetate Suspension; Philadelphia Laboratories, Inc., Division Philadelphia Pharmaceutical & Cosmetic Co., 9815 Roosevelt Blvd., Philadelphia, PA 19114.

12. NDA 10-255; Meticortelone Aqueous Suspension containing prednisolone acetate; Schering Corp., Galloping Hill Rd., Kenilworth, NJ 07033.

13. NDA 10-562; Hydextra-T.B.A. Suspension containing prednisolone butylacetate; Merck, Sharp & Dohme.

14. NDA 10-603; Cortisone Acetate Aqueous Suspension; Cooper Laboratories, 300 Fairfield Rd., Wayne, NJ 07470; successor to Vitamix Pharmaceuticals, Inc.

15. NDA 11-061; Meticortelone Soluble containing prednisolone sodium succinate; Schering Corp.

16. NDA 11-158; Deltacortril Aqueous Suspension containing prednisolone acetate; Pfizer Laboratories.

17. NDA 11-416; Sterane Aqueous Suspension containing prednisolone acetate; Pfizer Laboratories.

18. NDA 11-583; Hydextra Sol Injection containing prednisolone sodium phosphate; Merck, Sharp & Dohme.

19. NDA 11-685; Aristocort Intraleisional Suspension containing triamcinolone diacetate; Lederle Laboratories, Division of American Cynamid Co., P.O. Box 500, Pearl River, NY 10965.

20. NDA 11-757; That part of the NDA pertaining to Depo-Medrol Aqueous Suspension containing methylprednisolone acetate; The Upjohn Co.

21. NDA 11-856; Solu-Medrol Mix-O-Vial containing methylprednisolone sodium succinate; The Upjohn Co.

22. NDA 11-896; Prednisolone Acetate Suspension; Philadelphia Laboratories.

23. NDA 12-041; Kenalog Parenteral Aqueous Suspension containing triamcinolone acetonide; Squibb Pharmaceutical Co., Division of E. R. Squibb & Sons, Inc., P.O. Box 4000, Princeton, NJ 08540.

24. NDA 12-052; Hydrocortone Phosphate Injection containing hydrocortisone sodium phosphate; Merck Sharp & Dohme.

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

26. NDA 12-784; Cortiphate Injection containing hydrocortisone sodium phosphate; Travenol Laboratories, Inc., Morton Grove, IL 60053.

27. NDA 12-802; Aristocort Forte Suspension containing triamcinolone diacetate; Lederle Laboratories.

The following drugs were not included in the February 19, 1972 notice, but are affected by this notice:

1. NDA 8-856; Hydrocortone Concentrate Injection containing hydrocortisone; Merck Sharp & Dohme.

2. NDA 14-694; Hexadrol Phosphate Injection containing dexamethasone phosphate; Organon, Inc., Division of Akzona, Inc., 375 Mt. Pleasant Ave., West Orange, NJ 07052.

3. NDA 14-901; Kenalog-IM Injection containing triamcinolone acetonide; Squibb Pharmaceutical Co.

4. NDA 16-466; Aristospan Injection containing triamcinolone hexacetonide; Lederle Laboratories.

5. NDA 16-675; Decadron-LA Suspension/Injection containing dexamethasone acetate; Merck, Sharp & Dohme.

6. NDA 17-561; Celestone Phosphate Injection containing betamethasone sodium phosphate; Schering Corp.

Approval of the following three new drug applications, which were listed in the February 19, 1972 notice, had already been withdrawn on the ground of failure to submit required reports under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)). At the time the notices of withdrawal were published, no conclusions concerning the products' indications had been reached. Conclusions have now been

reached, and the purpose of including these new drug applications in this notice is to inform all interested persons of the conclusions and offer them the opportunity to request a hearing concerning all issues relating to the legal status of the products. In the listing that follows, the date and FEDERAL REGISTER citation identify the notice of withdrawal.

1. NDA 9-465; Hydrocortone-T.B.A. Suspension containing hydrocortisone butylacetate; Merck, Sharp & Dohme; October 27, 1971 (36 FR 20619).

2. NDA 10-291; Cortril Soluble Parenteral containing hydrocortisone sodium succinate; Pfizer Laboratories; August 6, 1971 (36 FR 14477).

3. NDA 10-650; Hydrocortisone Acetate; Cooper Laboratories (successor to Vitamix Pharmaceuticals, Inc.); February 8, 1972 (37 FR 2852).

Such 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 approved applications providing for such drugs. An approved new drug application is a requirement for marketing such drug products.

In addition to the holder(s) of the new drug application(s) specifically named above, this notice applies to all persons who manufacture or distribute a drug product, not the subject of an approved new drug application, that is identical, related, or similar to a drug product named above, as defined in 21 CFR 310.6. It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product he manufactures or distributes. Any person may request an opinion of the applicability of this notice to a specific drug product he manufactures or distributes that may be identical, related, or similar to a drug product named in this notice by writing to the Food and Drug Administration, Bureau of Drugs, Division of Drug Labeling Compliance (HFD-310), 5690 Fishers Lane, Rockville, MD 20857.

A. Effectiveness classification. The Food and Drug Administration has reviewed all available evidence and concludes that the drugs are effective for the indications listed in the labeling conditions below. Some of the indications appearing in the labeling conditions below did not appear in the previous notice. Having considered the information available concerning corticotropin and concerning the oral and parenteral glucocorticoids, the Director of the Bureau of Drugs concludes that, for the most part, when the dosage form and route of administration are appropriate, the same indications should be allowed for all.

The drug products named above now lack substantial evidence of effectiveness for the indications evaluated as probably effective and possibly effective in the February 19, 1972 notice.

B. Conditions for approval and marketing. 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 herein.

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

2. *Labeling conditions.* a. The label bears the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drugs are labeled to comply with all requirements of the act and regulations, and the labeling bears adequate information for safe and effective use of the drug. The indications are as follows:

A. *Intravenous or intramuscular administration.* 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.
- Hypercalcemia associated with cancer.

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, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy).
- Acute and subacute bursitis.
- Epicondylitis.
- Acute nonspecific tenosynovitis.
- Acute gouty arthritis.
- Psoriatic arthritis.
- Ankylosing spondylitis.

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.
- Mycosis fungoides.

5. *Allergic states.* Control of severe or incapacitating allergic conditions intrac-

table 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.
- Allergic conjunctivitis.
- Allergic corneal ulcers.

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

- Ulcerative colitis (systemic therapy).
- Regional enteritis (systemic therapy).

8. *Respiratory diseases:*

- Symptomatic sarcoidosis.
- Berylliosis.
- Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy.
- Loeffler's syndrome not manageable by other means.
- Aspiration pneumonia.

9. *Hematologic disorders:*

- Acquired (autoimmune) hemolytic anemia.
- Idiopathic thrombocytopenic purpura in adults (I.V. only; I.M. administration is contraindicated).
- Secondary thrombocytopenia in adults.
- Erythroblastopenia (RBC anemia).
- Congenital (erythroid) hypoplastic anemia.

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

- Leukemias and lymphomas in adults.
- Acute leukemia of childhood.

11. *Edematous states.* 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 used concurrently with appropriate antituberculous chemotherapy.
- Trichinosis with neurologic or myocardial involvement.

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.

B. *Intra-articular or soft tissue administration.* When the strength and dosage form of the drug lend the preparation to the treatment of the condition, these 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.
- Post-traumatic osteoarthritis.

C. *Intralesional administration.* 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 also may be useful in cystic tumors of an aponeurosis or tendon (ganglia).

3. *Marketing status of approved products.* Marketing of such drug products that are now the subject of an approved or effective new drug application may be continued provided that, on or before 60 days after date of publication in the FEDERAL REGISTER, the holder of the application submits the following if he has not previously done so: (i) a supplement for revised labeling as needed to be in accord with the labeling conditions described in this notice, and complete container labeling if current container labeling has not been submitted, and (ii) a supplement to provide updating information with respect to items 6 (components), 7 (composition), and 8 (methods, facilities, and controls) of new drug application form FD-356H (21 CFR 314.1(c)) to the extent required in abbreviated applications (21 CFR 314.1(f)).

4. *Marketing status of all other products.* a. Approval of an abbreviated new drug application must be obtained prior to marketing such product. The application shall contain the information specified in 21 CFR 314.1(f) and, for a suspension form product, shall include data of the kind required for this drug at the time of submission of the application to show that it is biologically available in the formulation proposed for marketing.

b. Marketing prior to approval of a new drug application will subject such products, and those persons who caused the products to be marketed, to regulatory action.

C. *Notice of opportunity for hearing.* On the basis of all the data and information available to him, the Director of the Bureau of Drugs is unaware of any adequate and well-controlled clinical investigation, conducted by experts qualified by scientific training and experience, meeting the requirements of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and 21 CFR 314.111(a)(5), demonstrating the effectiveness of the drug(s) for the indication(s) lacking substantial evidence of effectiveness referred to in paragraph A. of this notice.

Notice is given to the holder(s) of the new drug application(s), and to all other interested persons, that the Director of the Bureau of Drugs proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of the new drug application(s) (or, if indicated above, those part of the application(s) providing for the drug product(s) listed above) and all amendments and supplements thereto providing for the indication(s) lacking substantial evidence of effectiveness referred to in paragraph A. of this notice on the ground that new information before him with respect to the drug product(s), evaluated together with the evidence available to him at the time of approval of the application(s), shows there is a lack of substantial evidence that the drug product(s) will have all the effects it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling. An order withdrawing approval will not issue with respect to any application(s) supplemented, in accord with this notice, to delete the claim(s) lacking substantial evidence of effectiveness.

In addition to the ground for the proposed withdrawal of approval stated above, this notice of opportunity for hearing encompasses all issues relating to the legal status of the drug products subject to it (including identical, related, or similar drug products as defined in 21 CFR 310.6), e.g., any contention that any such product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act or because it is exempt from part or all of the new provisions of the act pursuant to the exemption for products marketed prior to June 25, 1938, contained in section 201(p) of the act, or pursuant to section 107(c) of the Drug Amendments of 1962; or for any other reason.

In accordance with the provisions of section 505 of the act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Parts 310, 314), the applicant(s) and all other persons who manufacture or distribute a drug product which is identical, related, or similar to a drug product named above (21 CFR 310.6), are hereby given an opportunity for a hearing to show why approval of the new drug application(s) providing for the claim(s) involved should not be withdrawn and an opportunity to raise, for administrative determination, all issues relating to the legal status of a drug product named above and all identical, related, or similar drug products.

If an applicant or any person subject to this notice pursuant to 21 CFR 310.6 elects to avail himself of the opportunity for a hearing, he shall file (1) on or before March 31, 1977, a written notice of appearance and request for hearing, and (2) on or before May 2, 1977, the data, information, and analyses on which he relies to justify a hearing, as specified in 21 CFR 314.200. Any other inter-

ested person may also submit comments on this proposal to withdraw approval. The procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, a submission of data, information, and analyses to justify a hearing, other comments, and a grant or denial of hearing, are contained in 21 CFR 314.200.

The failure of an applicant or any other person subject to this notice pursuant to 21 CFR 310.6 to file timely written appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by such person not to avail himself of the opportunity for a hearing concerning the action proposed with respect to such drug product and a waiver of any contentions concerning the legal status of such drug product. Any such drug product labeled for the indication(s) lacking substantial evidence of effectiveness referred to in paragraph A. of this notice may not thereafter lawfully be marketed, and the Food and Drug Administration will initiate appropriate regulatory action to remove such drug products from the market. Any new drug product marketed without an approved NDA is subject to regulatory action at any time.

A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for the hearing that there is no genuine and substantial issue of fact which precludes the withdrawal of approval of the application, or when a request for hearing is not made in the required format or with the required analyses, the Commissioner will enter summary judgment against the person(s) who requests the hearing, making findings and conclusions, denying a hearing.

II. Corticosteroid Products Especially Formulated for Rectal Administration and Approved Subsequent to October 9, 1962.

1. NDA 16-199; Cortenema, containing hydrocortisone; Rowell Laboratories, Inc., Lake of the Woods, Baudette, MN 56623.

2. NDA 11-757; That part of the NDA pertaining to Medrol Enpak, containing methylprednisolone acetate; The Upjohn Company, 7000 Portage Rd., Kalamazoo, MI 49001.

3. ANDA 85-023; Rectoid, containing hydrocortisone; Pharmacia Laboratories, 800 Centennial Ave., Piscataway, NJ 08854.

It is recognized that corticosteroids are effective in ulcerative colitis when administered systemically. The rationale for a topical product applied directly to the large bowel is that by exerting a topical effect it will be beneficial in ulcerative colitis but will produce less toxicity than would be produced by systemic treatment. Therefore, a rectally administered corticosteroid should not be absorbed to such

an extent that all of its beneficial effects are accounted for by the systemic dose achieved.

On the basis of information now available to the Food and Drug Administration, the present status and further requirements concerning these three products are as follows:

A. NDA 16-199 (Cortenema) (hydrocortisone). The effectiveness of this product as a topical agent is supported by absorption studies, clinical studies, and the literature, indicating that the amount of hydrocortisone absorbed is not sufficient to account for the beneficial therapeutic effects seen. No further studies are required at this time. If new information becomes available on rectal absorption of hydrocortisone which indicates that substantially more hydrocortisone reaches the systemic circulation than previous studies indicate, additional studies of this product may be required.

B. NDA 11-757 supplement (Medrol Enpak) (methylprednisolone acetate). This product was approved on the basis of studies showing satisfactorily low absorption. However, new information concerning the rectal absorption of prednisolone acetate suggests that rectal absorption of methylprednisolone acetate is likely to be substantially greater than heretofore shown for Medrol Enpak. The Director of the Bureau of Drugs concludes that the NDA holder should conduct additional bioavailability studies on that product, comparing it with oral methylprednisolone acetate. Depending upon the results, new clinical trials may be required to demonstrate that the therapeutic effect of Medrol Enpak is substantially topical and not systemic.

It is required that the results of such studies be submitted as a supplement to the application to the Division of Oncology and Radiopharmaceutical Drug Products (HFD-150), Bureau of Drugs, address given below, on or before (insert date 180 days after date of publication in the FEDERAL REGISTER).

C. ANDA 85-023 (Rectoid) (hydrocortisone). This was approved as an abbreviated new drug application. Because of the now recognized potential for wide variability in the extent of absorption of rectally administered corticosteroids, the Director of the Bureau of Drugs concludes that the NDA holder should conduct bioavailability studies comparing the product with Cortenema, for which a satisfactorily low degree of rectal absorption has been shown. The Director further concludes that, because of the known potential for variable absorption of rectally administered corticosteroids, and the possible requirement for clinical studies to assure effectiveness, abbreviated NDA's are not appropriate for such products. Accordingly, this abbreviated new drug application is to be converted to a full new drug application. It is required that the results of the bioavailability studies be submitted as a supplement to the full new drug application

to the Division of Oncology and Radiopharmaceutical Drug Products (HFD-150), Bureau of Drugs, address given below, on or before August 29, 1977.

The Bureau of Drugs will review the supplements received pursuant to the above requirements and inform the holders of the applications of its conclusions. If new information becomes available in the future concerning the rectal absorption of corticosteroids, e.g., if the state-of-the-art for measurement of rectal absorption improves, then additional studies by all NDA holders of these drug products will be required.

An approved full new drug application is a requirement for marketing of such products that are not now the subject of either an approved full new drug application or currently approved abbreviated new drug application. Full new drug application requirements are as follows:

(a) For a product in which the corticosteroid is identical to the corticosteroid contained in a marketed product for rectal administration that is provided for in an approved original full new drug application, data demonstrating bioequivalence to such approved product may be sufficient. If bioequivalence data are satisfactory, clinical studies will not ordinarily be required.

(b) For a product in which the corticosteroid does not have an identical counterpart in a marketed product for rectal administration that is provided for in an approved original full new drug application, bioavailability studies are required comparing the rectally administered product with a suitably formulated orally administered product of the same corticosteroid. Clinical studies are also required in order to demonstrate that the product is effective under the recommended conditions of dosage and administration. If the effectiveness of the rectally administered product clearly cannot be accounted for by the amount of corticosteroid absorbed, no further studies would be required. If this is not clear, additional studies would be required comparing rectal administration to oral administration of the same dose that is absorbed following rectal administration to establish that there is a true topical effect and that the full effectiveness of the product cannot be attributed to systemic absorption.

Marketing prior to approval of a new drug application will subject such products, and those persons who caused the products to be marketed, to regulatory action.

All submissions pursuant to this notice of opportunity for hearing shall be filed in quintuplicate. Such submissions, except for data and information prohibited from public disclosure pursuant to 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the office of the Hearing Clerk (address given below) between the hours of 9 a.m. and 4 p.m., Monday through Friday.

Communications forwarded in response to this notice should be identified with the reference number DESI 7110,

directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Supplements (identify with NDA number): Division of Oncology and Radiopharmaceutical Drug Products (HFD-150), Rm. 17B-34, Bureau of Drugs.

Original full new drug applications: Division of Oncology and Radiopharmaceutical Drug Products (HFD-150), Rm. 17B-34, Bureau of Drugs.

Original abbreviated new drug applications (identify as such): Division of Generic Drug Monographs (HFD-530), Bureau of Drugs.

Request for Hearing (identify with Docket number appearing in the heading of this notice): Hearing Clerk, Food and Drug Administration (HFC-20), Rm. 4-65.

Requests for the report of the National Academy of Sciences-National Research Council: Public Records and Document Center (HFC-18), Rm. 4-62.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFD-501), Bureau of Drugs.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-1053, as amended (21 U.S.C. 352, 355)) and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.31) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)).

Dated: February 18, 1977.

J. RICHARD CROUT,
Director, Bureau of Drugs.

[FR Doc. 77-6041 Filed 2-28-77; 8:45 am]

[Docket No. 76N-0227; DESI 763]

LIDOCAINE HYDROCHLORIDE 2 PERCENT VISCOSUS

Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice and Opportunity for Hearing

In a notice (DESI 763; Docket No. FDC-D-272 (now Docket No. 76N-0227)) published in the FEDERAL REGISTER of April 10, 1971 (36 FR 6909), the Food and Drug Administration (FDA) announced its conclusions that the drug described below is effective for providing symptomatic relief of pain when applied to irritated or inflamed mucous membranes of the mouth and pharynx. The drug product was also certified as possibly effective for certain other indications. After a reevaluation of the reports received from the National Academy of Sciences-National Research Council, FDA has determined that one of the possibly effective indications, the indication for relief of pain and discomfort of post-tonsillectomy sore throat, is encompassed in the effective indication as worded in the April 10, 1971 notice. No person has submitted any data in support of the remaining possibly effective indications, and they

are now reclassified as lacking substantial evidence of effectiveness. This notice offers an opportunity for a hearing concerning those indications and states the conditions for marketing such drugs for the indication classified as effective. Persons who wish to request a hearing may do so on or before March 31, 1977. Other products named in the April 10, 1971 notice are not affected by this notice.

NDA 9-470; Xylocaine Viscous containing lidocaine hydrochloride 2 percent; Astra Pharmaceutical Products, Inc., 7 Neponset St., Worcester, MA 01606.

Such 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. An approved new drug application is a requirement for marketing such drug products.

In addition to the holder(s) of the new drug application(s) specifically named above, this notice applies to all persons who manufacture or distribute a drug product, not the subject of an approved new drug application, that is identical, related, or similar to a drug product named above, as defined in 21 CFR 310.6. It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product he manufactures or distributes. Any person may request an opinion of the applicability of this notice to a specific drug product he manufactures or distributes that may be identical, related, or similar to a drug product named in this notice by writing to the Food and Drug Administration, Bureau of Drugs, Division of Drug Labeling Compliance (HFD-310), 5600 Fishers Lane, Rockville, MD 20857.

A. *Effectiveness classification.* The Food and Drug Administration has reviewed all available evidence and concludes that the drug is effective for the indication listed in the labeling conditions below and lacks substantial evidence of effectiveness for all its other labeled indications not encompassed, as discussed above, in the effective indication.

B. *Conditions for approval and marketing.* 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 herein.

1. *Form of drug.* Lidocaine hydrochloride 2 percent viscous is in solution form suitable for topical application.

2. *Labeling conditions.* a. The label bears the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drug is labeled to comply with all requirements of the act and regulations, and the labeling bears adequate information for safe and effective use of the drug. The Indication is as follows:

For the production of topical anes-

committee of the Food and Drug Administration (FDA). This notice also sets forth a summary of the procedures governing committee meetings and methods by which interested persons may participate in open public hearings conducted by the committees and is issued under section 10(a) (1) and (2) of the Federal Advisory Committee Act (Pub. L. 92-463,

86 Stat. 770-776 (5 U.S.C. App. I)), and FDA regulations (21 CFR Part 14) (formerly Subpart D of Part 2 prior to recodification published in the FEDERAL REGISTER of March 22, 1977 (42 FR 15553)) relating to advisory committees. The following advisory committee meeting is announced:

on Laetrile will begin at 9 a.m. on May 2, 1977, in the Royal Hall of the Radisson Muehlebach Hotel, 12th and Baltimore Streets, Kansas City, MO.

FOR FURTHER INFORMATION CONTACT:

Tenny P. Neprud, Compliance Regulation Policy Staff (HFC-10), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, (301) 443-3480.

Committee name	Date, time, and place	Type of meeting and contact person
Oncologic Drugs Advisory Committee.	April 12 and 13, conference room F, Parklawn Bldg., 5600 Fishers Lane, Rockville, Md.	Open public hearing April 12, 9 a.m. to 10 a.m.; open committee discussion April 12, 10 a.m. to 4:30 p.m., April 13, 9 a.m. to 3 p.m.; Cyrus H. Maxwell, M.D. (HFD-150), 5600 Fishers Lane, Rockville, Md. 20857, 301-443-5197.

SUPPLEMENTARY INFORMATION: In the FEDERAL REGISTER of February 18, 1977 (42 FR 10066), the Commissioner, pursuant to court order, announced the commencement of a rulemaking proceeding to compile an administrative record concerning the "new drug" and "grandfather" status of the cancer drug Laetrile, set forth instructions and other information for those persons who desire to submit initial and reply testimony and requests to present oral argument and stated that oral argument concerning the medical and legal significance of the testimony would be held on May 2, 1977, at Kansas City, MO. at a time and place to be designated in the FEDERAL REGISTER at a later date.

Dated: March 21, 1977.

JOSEPH P. HILE,
Associate Commissioner for Compliance.

[FR Doc.77-8958 Filed 3-24-77;8:45 am]

[Docket No. 76N-1227; DESI 763]
LIDOCAINE HYDROCHLORIDE 2 PERCENT VISCOUS

Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice and Opportunity for Hearing

Correction

In FR Doc. 77-6038 appearing at page 11897 in the issue for Tuesday, March 1, 1977, the word "certified" in the 12th line of the document should have read "classified".

[Docket No. 76P-0224]

RCA CORP.

Approval of Variance for Laser Range Po System

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: This notice announces that a variance from § 1040.11(b) (21 CFR 1040.11(b)) of the performance standard for laser products has been approved by the Director, Bureau of Radiologic Health, Food and Drug Administration. EFFECTIVE DATE: April 25, 1977. Termination, April 25, 1982.

ADDRESS: Written objections and supporting data to the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

General function of the committee. Review and evaluates available data concerning the safety and effectiveness of marketed and investigational prescription drugs for use in the treatment of cancer.

Agenda—Open public hearing. Any interested persons may present data, information, or views, orally or in writing, on issues pending before the committee.

Open committee discussion. Discussion of IND 945 (Hexamethylmelanine), IND 8041 (Cis-Diamminedichloroplatinum II); National Cancer Institute (NCI) program of distribution of investigational new drugs.

FDA public advisory committee meetings may have as many as four separable portions: (1) An open public hearing, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. There are no closed portions for the meetings announced in this notice. The dates and times reserved for the open portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairman determines will facilitate the committee's work.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this FEDERAL REGISTER notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hear-

ing's conclusion, if time permits, at the chairman's discretion.

Persons interested in specific agenda items to be discussed in open session may ascertain from the contact person the approximate time of discussion.

A list of committee members and summary minutes of meetings may be obtained from the Public Records and Documents Center (HFC-18), 5600 Fishers Lane, Rockville, MD 20857, between the hours of 9 a.m. and 4 p.m., Monday through Friday. The FDA regulations relating to public advisory committees may be found in 21 CFR Part 14 (formerly Subpart D of Part 2), prior to recodification published in the FEDERAL REGISTER of March 22, 1977 (42 FR 15553).

Dated: March 18, 1977.

WILLIAM F. RANDOLPH,
Acting Associate
Commissioner for Compliance.

[FR Doc.77-8672 Filed 3-24-77;8:45 am]

[Docket No. 76N-0328; DESI 7110]

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

Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice and Opportunity for Hearing

Correction

In FR Doc. 77-6041 appearing at page 11893 in the issue for Tuesday, March 1, 1977, make the following corrections:

(1) On page 11895, in the third column, in the 6th line of the paragraph numbered "3", the date 60 days from publication is May 2, 1977.

(2) On page 11896, in the third column, the 4th full paragraph, the date 180 days from publication is August 29, 1977.

[Docket No. 77N-0048]

LAETRILE

Oral Argument

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Commissioner of Food and Drugs announces that oral argument

the Secretary, Board of Governors of the Federal Reserve System, Washington, D.C. 20551, to be received no later than June 20, 1977. If a request for oral hearing is filed, each request should contain a statement of the nature of the requesting person's interest in the matter, his reasons for wishing to appear at an oral hearing, and a summary of the matters concerning which such person wishes to give testimony. The Board subsequently will designate a time and place for any hearing it orders, and will give notice of such hearing to the transferor, the transferee, and all persons that have requested an oral hearing. In the absence of a request for an oral hearing, the Board will consider the requested determination on the basis of documentary evidence filed in connection with the application.

Board of Governors of the Federal Reserve System, May 23, 1977.

GRIFFITH L. GARWOOD,
Deputy Secretary of the Board.
[FR Doc.77-15162 Filed 5-26-77;8:45 am]

GENERAL ACCOUNTING OFFICE REGULATORY REPORTS REVIEW

Receipt of Report Proposal

The following request for clearance of a report intended for use in collecting information from the public was received by the Regulatory Reports Review Staff, GAO, on May 20, 1977. See 44 U.S.C. 3512 (c) and (d). The purpose of publishing this notice in the FEDERAL REGISTER is to inform the public of such receipt.

The notice includes the title of the request received; the name of the agency sponsoring the proposed collection of information; the agency form number, if applicable; and the frequency with which the information is proposed to be collected.

Written comments on the proposed FEA request are invited from all interested persons, organizations, public interest groups, and affected businesses. Because of the limited amount of time GAO has to review the proposed request, comments (in triplicate) must be received on or before June 10, 1977, and should be addressed to Mr. John M. Lovelady, Acting Assistant Director, Regulatory Reports Review, United States General Accounting Office, Room 5033, 441 G Street, NW., Washington, D.C. 20548.

Further information may be obtained from Patsy J. Stuart of the Regulatory Reports Review Staff, 202-275-3532.

FEDERAL ENERGY ADMINISTRATION

FEA requests clearance of its new, semi-annual Form FEA-U524-P-O entitled Industrial Energy Conservation and Consumption Report. The FEA-U524-P-O is required by Section 375 of art D of Title II of the Energy Policy

and Conservation Act (EPCA) (Pub. L. 94-163). The FEA-U524-P-O provides the means for monitoring the progress by industry towards conservation targets set by FEA in accordance with Section 374 of the EPCA. FEA estimates respondents to the FEA-U524-P-O to number approximately 130 corporations and burden to average 30 hours per response.

NORMAN F. HEYL,
Regulatory Reports,
Review Officer.

[FR Doc.77-15103 Filed 5-26-77;8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration
[Docket No. 77G-0099]

ARTHUR A. CHECCHI, INC.

Filing of Petition for Affirmation of GRAS Status

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: A petition has been filed by Arthur A. Checchi, Inc., proposing affirmation that high-fructose corn syrup prepared by converting a part of the glucose in corn syrup to fructose by glucose isomerase enzyme, derived from *Bacillus coagulans*, for use as a sweetener in foods and the glucose isomerase enzyme are GRAS.

DATE: Comments by July 26, 1977.

ADDRESS: Written comments to the Hearing Clerk (HFC-20), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Corbin I. Miles, Bureau of Foods (HFF-335), Food and Drug Administration, Department of Health, Education, and Welfare, 200 C St. SW., Washington, DC 20204, 202-472-4750.

SUPPLEMENTARY INFORMATION: Pursuant to provisions of the Federal Food, Drug and Cosmetic Act (secs. 201(s), 409, 701(a), 52 Stat. 1055, 72 Stat. 1784-1788 (21 U.S.C. 321(s), 348, 371(a))) and the regulations for affirmation of Grasp status in § 170.35 (21 CFR 170.35, formerly § 121.40, prior to recodification published in the FEDERAL REGISTER of March 15, 1977 (42 FR 14302)), notice is given that a petition (GRASP 7G0086) has been filed by Arthur A. Checchi, Inc., 1730 Rhode Island Ave. NW., Washington, D.C. 20036, and placed on public display at the office of the Hearing Clerk, Food and Drug Administration, proposing affirmation that high-fructose corn syrup prepared by converting a part of the glucose in corn syrup to fructose by glucose isomerase enzyme, derived from *Bacillus coagulans*, for use as a sweetener in foods and the glucose isomerase enzyme are GRAS.

Any petition which meets the format requirements outlined in § 170.35 is filed by the Food and Drug Administration. There is no pre-filing review of the adequacy of data to support a GRAS conclusion. Thus the filing of a petition for GRAS affirmation should not be interpreted as a preliminary indication of suitability for affirmation.

Interested persons may, on or before July 26, 1977, review the petition and/or file comments (in quadruplicate) with the Hearing Clerk (HFC-20), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857. Comments should include any available information that would be helpful in determining whether the substance is, or is not, generally recognized as safe. A copy of the petition and received comments may be seen in the office of the Hearing Clerk, address given above, between the hours of 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 18, 1977.

HOWARD R. ROBERTS,
Acting Director,
Bureau of Foods.

[FR Doc. 77-15095 Filed 5-26-77;8:45 am]

[Docket No. 76N-0406; DESI 7504]

CORTICOTROPIN FOR PARENTERAL USE

Drugs For Human Use; Drug Efficacy Study Implementation Amended Followup Notice

AGENCY: Food and Drug Administration.

ACTION: Amended notice.

SUMMARY: This notice amends a notice published in the FEDERAL REGISTER of March 1, 1977, to correct the omission of an indication for use of parenteral corticotropin, to change the name of one of the new drug application holders, and to correct two other errors.

ADDRESSES: Communications forwarded in response to this notice should be identified with the reference number DESI 7504; directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20857.

Supplements (identify with NDA number): Division of Metabolism and Endocrine Drug Products (HFD-130), Rm. 14B-03, Bureau of Drugs.

Original abbreviated new drug applications (identify as such): Division of Generic Drug Monographs (HFD-530), Bureau of Drugs.

Request for Hearing (identify with Docket number appearing in the heading of this notice): Hearing Clerk, Food and Drug Administration (HFC-20), Rm. 4-65.

Requests for the report of the National Academy of Sciences-National Research Council: Public Records and Document Center (HFC-18), Rm. 4-62.

Requests for opinion of the applicability of this notice to a specific product: Division of Drug Labeling Compliance (HFD-310), Bureau of Drugs.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFD-501), Bureau of Drugs.

FOR FURTHER INFORMATION CONTACT:

John H. Hazard, Jr., Administrative Compliance Branch (HFD-32), Office of the Assistant Director for Regulatory Affairs, Bureau of Drugs, Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, Md. 20857 (301-443-3650).

SUPPLEMENTARY INFORMATION: In a notice (DESI 7504) published in the FEDERAL REGISTER of March 1, 1977 (42 FR 11891), several inadvertent errors appeared in the indications section on page 11892 in the third column: In item 10, "Edematous states," the phrase "the idiopathic" should be inserted before the word "type." In item 12, "Miscellaneous," the words "concurrent by" should read "concurrently." Also under "Miscellaneous," the following indication should be added:

Trichinosis with neurologic or myocardial involvement.

In addition, the notice incorrectly stated that the holder of NDA 12-089, Purified Corticotropin-Gel/Injection was Elkins-Sinn, Inc., 2 Easterbrook Ln., Cherry Hill, NJ 08002. The holder of the NDA should be listed as Philadelphia Laboratories, Inc., formerly of 9815 Roosevelt Blvd., Philadelphia, PA 19114.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-1053, as amended (21 U.S.C. 352, 355)) and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.82) (recodification published in the FEDERAL REGISTER of March 22, 1977 (42 FR 15553)).

Dated: May 10, 1977.

CARL M. LEVENTHEL,
Acting Director,
Bureau of Drugs.

[FR Doc. 77-14961 Filed 5-26-77; 8:45 am]

[Docket No. 77C-0126]

COSMETIC, TOILETRY, AND FRAGRANCE ASSOCIATION, INC.**Color Additive Petitions**

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: Pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (sec. 706(d), 74 Stat. 402 (21 U.S.C. 376(d))), notice is given that color additive petitions (CAP's) have been filed by the Cosmetic, Toiletry, and Fragrance Association, Inc., 1130 15th St., NW., Washington, DC 20005, proposing the issuance of color additive regulations (21 CFR Part 73) to provide for the safe use and exemption from certification of the color additives specified below.

FOR FURTHER INFORMATION CONTACT:

Gerard McCowin, Bureau of Foods (HFF-334), Food and Drug Administration, Department of Health, Education, and Welfare, 200 C St. SW., Washington, D.C. 20204. (202-472-5740).

SUPPLEMENTARY INFORMATION:
The submitted color additive petitions are as follows:

CAP No.	Color additives	Uses
6C0117	Aluminum powder.	In externally applied drugs and externally applied cosmetics including those used in the area of the eye.
6C0118	Annatto....	In externally applied drugs and in cosmetics, generally, including those used in the area of the eye.
6C0121	β -Carotene..	Do.
6C0122	Zinc oxide..	Do.

The environmental impact analysis report and other relevant material have been reviewed, and it has been determined that the proposed use of the additive will not have a significant environmental impact. Copies of the environmental impact analysis report may be seen in the office of the office of the Hearing Clerk, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, during working hours Monday through Friday.

Dated: May 3, 1977.

HOWARD R. ROBERTS,
Acting Director,
Bureau of Foods.

[FR Doc. 77-14964 Filed 5-26-77; 8:45 am]

[Docket No. 77F-0077]

GENERAL FOODS CORP.**Filing of Food Additive Petitions****Correction**

In FR Doc. 77-12971 appearing at page 23170 in the issue for Friday, May 6, 1977, the headings should read as set forth above.

[Docket No. 76N-0209; DESI 10070]

PANCREATIC DORNASE**Opportunity For Hearing on Proposal to Withdraw Approval of New Drug Application**

AGENCY: Food and Drug Administration.

ACTION: Notice.

DATES: Hearing requests due on or before June 27, 1977.

SUMMARY: This notice reclassifies pancreatic dornase to lacking substantial evidence of effectiveness, proposes withdrawal of approval of the new drug application and offers an opportunity for a hearing on the proposal.

ADDRESSES: Communications forwarded in response to this notice should be identified with the reference number DESI 10070 and the docket number appearing in the heading of this notice, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Request for Hearing: Hearing Clerk, Food and Drug Administration (HFC-20), Rm. 4-65.

Request for opinion of the applicability of this notice to a specific product: Division of Drug Labeling Compliance (HFD-310), Bureau of Drugs, Food and Drug Administration.

FOR FURTHER INFORMATION CONTACT:

Herbert Gerstenzang, Bureau of Drugs (HFD-32), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857. (301-443-3650.)

SUPPLEMENTARY INFORMATION: In a notice (DESI 10070) published in the FEDERAL REGISTER of July 30, 1970 (35 FR 12232), the Food and Drug Administration (FDA) announced its conclusion that the drug product described below is less than effective (probably effective) as an adjunct in the treatment of paranasal sinus infections, for tracheitis sicca, cystic fibrosis of the pancreas, and for reducing tenacity of pulmonary secretions in bronchopulmonary infections; and is less than effective (possibly effective) for its other labeled indications.

NDA 10-070; Dornavac Powder containing pancreatic dornase for inhalation or irrigation; Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19486.

Pursuant to the notice of July 30, 1970, Merck, Sharp & Dohme submitted data from three clinical studies. The studies are discussed below.

Dr. M. J. Dulfano evaluated the effect of pancreatic dornase on 30 male patients (14 on pancreatic dornase and 16 on placebo) who were suffering from an acute exacerbation of chronic bronchitis and had a mucopurulent sputum. The drug was administered twice daily for 3 days, and the investigator assessed pulmonary function by chest X-ray examinations and by determining the forced expiratory volume, the forced expiratory volume in 1 second, the maximum volume ventilation, and the maximum mid-expiratory flow. He also evaluated cough, dyspnea, and chest symptoms (all on a 3-point scale) and the sputum characteristics (quantity, viscosity in poises, elastic recoil in units, opacity on a 3-point scale, specific gravity, cell population on a 5-point scale, the cell differential, and bacteriology) before treatment, five times during the treatment, and once the day after the treatment was terminated. During the study two patients on Dornavac had to discontinue taking the drug, one because of wheezing and shortness of breath and the other because of the taste of the drug. Statistical analysis of the results by the sponsor indicated no significant differences in sputum characteristics and pulmonary function variables. The scores, however, for the chest symptoms during the last 2 days of the study showed a statistically significant difference in favor of the placebo. Merck Sharp & Dohme acknowledged that Dr. Dulfano's study did not show efficacy.

Dr. J. Bushnell evaluated the effect of pancreatic dornase on 40 patients (20 on pancreatic dornase and 20 on placebo) with paranasal sinus infection. The drug was administered once daily for 3 days, and the investigator assessed the results by X-ray examination, transillumination, and bacteriological cultures, and also by estimating the amount of discharge and pus in the sinus washings

and the degree of pain, swelling, and redness (on a 3-point scale) after each treatment. At the end he evaluated the overall effect of treatment (satisfactory or unsatisfactory). Statistical analysis of patient characteristics indicated that the two groups (20 placebo patients vs. 20 Dornavac patients) were comparable regarding age and sex, but they were not comparable in the duration of infection before the treatment was initiated, a critical variable that could affect the rate of healing and resolution of symptoms. 21 CFR 314.111(a)(5)(ii)(a)(2)(iii). The average duration of illness before treatment was started was 1.5 weeks in the Dornavac group, while it was 3 to 5 weeks in the placebo group ($p < 0.05$). The results of this study indicated that there were no significant differences between the two groups regarding any of the parameters except that the Dornavac group felt less pain after the first treatment than did the placebo group ($p = 0.04$) so that the reduction of pain from the pretreatment level was greater in this group ($p = 0.1$). However, there were no significant differences in pain between the groups after the second and third treatments. In addition, the X-ray examinations indicated that more placebo patients had both antra clear at the second examination ($p = 0.08$). In view of the fact that the placebo group and Dornavac group differed with respect to duration of illness, a critical variable it cannot be concluded that the initial faster reduction of pain in the Dornavac group indicates drug effectiveness. Merck Sharp & Dohme acknowledged that the Bushnell study did not demonstrate effectiveness.

Dr. W. E. Loch treated 16 patients suffering from sinusitis with Dornavac and 15 others with placebo in a claimed randomized double-blind parallel design for a period of 4 days. The sponsor claims that the treatment groups were comparable in age and sex, presence of local discharge prior to the study, presence of headaches, past history, and use of other therapies for headaches during the study, although significant pretreatment differences were observed in the frequency of allergy, use of regular pre-study medication, and presence of headaches influenced by cough. The investigator assessed the results by physical examinations, bacteriological cultures, nasal photographs, X-rays, and rhinometry. Observations were made of the patients' progress at each of the four treatment days and at a followup day 1 to 2 weeks after the last treatment. The investigator found that the patients who were treated with Dornavac had significantly more improvement in nasal discharges, swelling, and redness than did the patients treated with the placebo, and that this improvement was evidenced also in nasal photographs of the affected sinuses which were taken before and after treatment. The investigator also commented that treatment with Dornavac was satisfactory in all patients in all four evaluation periods, while treatment with placebo was unsatisfactory in all cases in all evaluation

periods except in the last period for one patient, when he found the treatment satisfactory.

Copies of the nasal photographs have never been submitted to the agency. However, these were reevaluated for Merck Sharp & Dohme by Dr. James Snow, Jr., who found no significant differences between the Dornavac and the placebo group regarding the disappearance of the exudate. Similarly, reevaluation of the X-ray reports by FDA and by the sponsor showed no significant differences between the groups regarding improvement of the sinus condition. In addition, blind reevaluation of the original X-ray films by Dr. Wallace T. Miller at the request of the sponsor revealed no differences. Also not supportive of effectiveness were the results of the (a) bacteriological cultures, which showed no significant differences between the groups in the type, number, and sensitivity of the cultured bacteria to six antibiotics, and (b) rhinometry. The rhinograms, as reported by the sponsor, showed improvement only in two of the 16 Dornavac patients and in one of the 15 placebo patients. These results give a valuable of $p > 0.5$.

The experimental and placebo groups in this study were not comparable regarding condition treated. 21 CFR 314.111(a)(5)(ii)(a)(2)(iii). Five patients in the placebo group had chronic pansinusitis that had lasted from 11 months to 8 years, with recurrent exacerbations. In five other placebo patients the pansinusitis was superimposed on viral infections. None of the 15 placebo patients had allergic manifestations at the time of the study, and only five of them had a history of allergy. In contrast, only two of the patients treated with Dornavac had chronic sinusitis, which had been of rather short duration (4 and 9 months respectively), and only one Dornavac patient had a viral infection. In further contrast, five Dornavac patients had allergic rhinitis during the period of the study while an additional six patients had a history of allergy, making a total of 11 Dornavac patients who had a history of allergy. Since allergic reactions can subside without treatment once the offending antigen is eliminated, the Dornavac-treated patients as a group were in a more favorable condition than the placebo patients in addition to having fewer chronic sinusitides to start with.

In this study the investigator's subjective evaluations of the patients' symptoms are in sharp contrast with the objective criteria and suggest that observer or analyst bias could have been present, perhaps because of breakdown of double-blind conditions. 21 CFR 314.111(a)(5)(ii)(a)(4). Included with the protocol that was sent to the investigator was a chart that divided the medication numbers into two groups and identified them as Dornavac and placebo. It appears, therefore, that the study was not blind at all, at least for the investigator, who received a copy of the protocol before he treated any pa-

tient. His knowledge of the allocation schedule can explain the discrepancies between his subjective evaluations and the objective criteria of the study.

In summary, the Loch study cannot be considered adequate and well controlled and does not support the claim that the drug product is effective for the claimed indications.

On the basis of all of the data and information available to him, the Director of the Bureau of Drugs is unaware of any adequate and well controlled clinical investigation, conducted by experts qualified by scientific training and experience, meeting the requirements of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and 21 CFR 314.111(a)(5), demonstrating the effectiveness of the drug.

Therefore, notice is given to the holder(s) of the new drug application(s) and to all other interested persons that the Director of the Bureau of Drugs proposes to issue an order under section 505 (e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of the new drug application(s) (or if indicated above, those parts of the application(s) providing for the drug product(s) listed above) and all amendments and supplements thereto on the ground that new information before him with respect to the drug product(s) evaluated together with the evidence available to him at the time of approval of the application(s), shows there is a lack of substantial evidence that the drug product(s) will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling.

In addition to the holder(s) of the new drug application(s) specifically named above, this notice of opportunity for hearing applies to all persons who manufacture or distribute a drug product which is identical, related, or similar to a drug product named above, as defined in 21 CFR 310.6. It is the responsibility of every drug manufacturer or distributor to review this notice of opportunity for hearing to determine whether it covers any drug product he manufactures or distributes. Any person may request an opinion of the applicability of this notice to a specific drug product he manufactures or distributes that may be identical, related, or similar to a drug product named in this notice by writing to the Division of Drug Labeling Compliance (HFD-310), Bureau of Drugs.

In addition to the ground(s) for the proposed withdrawal of approval stated above, this notice of opportunity for hearing encompasses all issues relating to the legal status of the drug products subject to it (including identical, related, or similar drug products as defined in 21 CFR 310.6) e.g., any contention that any such product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act or because it is exempt from part or all of the new drug provisions of the act pursuant to the exemption for products marketed prior to June 25, 1938, contained in section 201(p) of the act, or

MEMO RECORD	AVOID ERRORS PUT IT IN WRITING	DATE 6-10-77
FROM: J. Taylor (thru J.L. Meyer)		OFFICE HFD-530
TO: Mr. David H. Bryant, Office of Compliance		DIVISION HFD-322
SUBJECT: Inspection Request		
<p>SUMMARY In connection with ANDA 81-825, (b) (4) Triamcinolone Acetonide Suspension 40mg for: (b) (4)</p> <p>Applicant: Carter - Glogau Laboratories Division Chromalloy Pharmaceuticals, Inc. 5160 W. Bethany Home Road Glendale, AZ 85301</p> <p>AF -</p> <p>REQUESTED:</p> <p><input checked="" type="checkbox"/> 1. Evaluation of compliance with CGMP for:</p> <p style="margin-left: 40px;"><input type="checkbox"/> a. The applicant</p> <p style="margin-left: 40px;"><input checked="" type="checkbox"/> b. Others All laboratory tests are performed by (b) (4)</p> <p><input checked="" type="checkbox"/> 2. Recommendation for approval/disapproval of the application/communication/supplement, based on your evaluation of compliance with CGMP</p> <p>REMARKS:</p>		
SIGNATURE C. Gray	DOCUMENT NUMBER 81-825, (b) (4)	

JUN 24 1977

NDA 85-825

Carter-Glogau Laboratories Division
Chromalloy Pharmaceuticals, Inc.
Attention: Dr. Samuel Fainberg
5160 West Bethany Home Road
Glendale, AZ 85301

Gentlemen:

Reference is made to your abbreviated new drug application dated May 9, 1977, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triamcinolone Acetonide Suspension, 40 mg. per ml.

We have completed the review of this abbreviated new drug application and have the following comments:

1. Submit the appropriate Drug Master File referral for (b) (4)
2. (b) (4)
3. Submit the currently available stability data with methodology.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 6/24/77
Marvin Seife, M.D.
Director

Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs

R. Barzilai 6/22/77

cc: LOS-DO
DUP HFD-614 HFD-616

XXXXXXXXXXXXXXXXXXXX
RBarzilai/JMeyer/JTaylor
r/d iit. JMeyer/MSeife 6-22-77

f/t/wlb/6-22-77
rev w/f JMeyer 6/23/77



CHROMALLOY PHARMACEUTICALS, INC.

A SUBSIDIARY OF CHROMALLOY AMERICAN CORPORATION

Drug

CARTER-GLOGAU LABORATORIES DIVISION

August 16, 1977

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education, and Welfare
Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA ORIG AMENDMENT

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 MG/ML
NDA 85-825

Dear Dr. Seife:

We hereby amend our NDA 85-825 for Triamcinolone Acetonide Suspension 40 mg/ml.

This amendment provides for (b) (4) as an additional supplier of the active ingredient.

There are no other changes or amendments to this NDA.

Sincerely yours,

CARTER-GLOGAU LABORATORIES DIVISION
CHROMALLOY PHARMACEUTICALS, INC.

Samuel M. Fainberg,
Director
Technical and Regulatory Affairs

SMF/jcw

GENERAL OFFICES:
5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301
TELEPHONE (602) 939-7565 • TELEX 66-8304 (M-C LABS)



NOV 10 1977

NDA 85-825

Carter-Glogau Laboratories Division
Chromalloy Pharmaceuticals, Inc.
Attention: Dr. Samuel Fainberg
5160 W. Bethany Home Road
Glendale, AZ 85301

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triamcinolone Acetonide Suspension, 40 mg. per ml.

We acknowledge receipt of your communication dated August 16, 1977.

We have re-reviewed this abbreviated new drug application and request the following additional information:

1. That requested per our letter of June 24, 1977.
2. An updated stability protocol to include:
 - a) particle size
 - b) crystalline form (presence of polymorphs)
 - c) resuspendability/sedimentation rate
 - d) syringabilitywith methodology and a commitment to withdraw any product demonstrating radical changes.
3. A commitment to submit additional stability data as it becomes available. In addition, our Division of Drug Manufacturing has the following comments regarding the proposed supplier (b) (4):

(b) (4) declines to be inspected at the present time. The referenced ANDA is therefore not approvable since there is insufficient information to assess the firm's compliance with Current Good Manufacturing Practice regulations.

Please let us have your response promptly.

cc:
LOS-DO
HFD-614
JMeyer/JTaylor *ps/11/9/77*
R/D init JMeyer/MSeife/11/9/77
ps/11/9/77
rev w/f
JMeyer 11/9/77

Sincerely yours,

for Dr. Seife
Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
11/10/77



CHROMALLOY PHARMACEUTICALS, INC.

A SUBSIDIARY OF CHROMALLOY AMERICAN CORPORATION

Drug

CARTER-GLOGAU LABORATORIES DIVISION

February 28, 1978

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education, and Welfare
Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA ORIG AMENDMENT

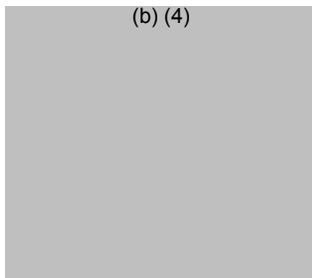
*No reply
required at this
time
Jules 3/22/78*

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 MG/ML
NDA 85-825

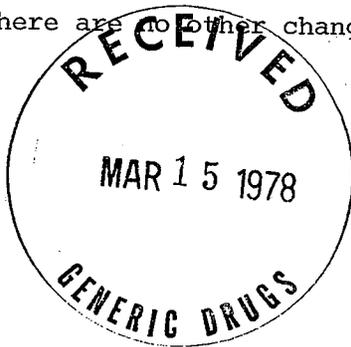
Dear Dr. Seife:

Reference is made to our NDA 85-825 for Triamcinolone Acetonide Suspension, 40 mg/ml.

We wish to withdraw the following suppliers of the active ingredient from the above referenced NDA:

(b) (4)


There are no other changes or additions to this NDA.



Sincerely yours,

CARTER-GLOGAU LABORATORIES DIVISION
CHROMALLOY PHARMACEUTICALS, INC.

Samuel M. Fainberg
Samuel M. Fainberg, Ph.D.
Director
Technical and Regulatory Affairs

SMF/jcw

GENERAL OFFICES:
5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301
TELEPHONE (602) 939-7565 • TELEX 66-8304 (M-C LABS)



CHROMALLOY PHARMACEUTICALS, INC.

A SUBSIDIARY OF CHROMALLOY AMERICAN CORPORATION

Drug

CARTER-GLOGAU LABORATORIES DIVISION

May 31, 1978

Marvin Seife, M.D.
 Director
 Division of Generic Drug Monographs
 Office of Drug Monographs
 Bureau of Drugs
 Department of Health, Education, and Welfare
 Public Health Service
 Food and Drug Administration
 Rockville, MD 20857

NO MEDICAL REVIEW INDICATED
 SIG: *[Signature]*
 DATE: *[Signature]*

RESUBMISSION

1/18/81
 NDA ORIG AMENDMENT

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 MG/ML
 NDA 85-825

Dear Dr. Seife:

Reference is made to your letters of June 24, 1977, July 27, 1978 and November 14, 1977 regarding Triamcinolone Acetonide Suspension, 40 mg/ml, NDA 85-825.

We are supplying the following as requested:

Regarding the June 24, 1977 letter:

1. (b)(4) was withdrawn as a supplier of the active ingredient in our correspondence of February 28, 1978.
2. Our Master Formula Card clarifying the procedure (b)(4)
3. As production lots become available we will place the initial three batches on stability with testing intervals at 3, 6, 9, 12, 18, 24, and 36 months. Any lot falling out of specifications will promptly be withdrawn from the market.

Regarding the July 27, 1977 letter:

1. Information requested in your letter of June 24, 1977 - See above.
2. Assay methodology is USP XIX.
3. Samples of the dosage form, lot number 78C025, and testing results are attached.

GENERAL OFFICES:
 5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301
 TELEPHONE (602) 939-7565 • TELEX 66-8304 (M-C LABS)



CHROMALLOY PHARMACEUTICALS, INC.

A SUBSIDIARY OF CHROMALLOY AMERICAN CORPORATION

CARTER-GLOGAU LABORATORIES DIVISION

Marvin Seife, M.D./Food and Drug Administration

page 2/NDA 85-825

May 31, 1978

Regarding the November 10, 1977 letter:

1. Information requested in your letter of June 24, 1977 is attached.
2. Our stability testing will include particle size, crystalline form, resuspendability, and syringeability in addition to assay for the active ingredient, benzyl alcohol and observance of the appearance. We will promptly withdraw from the market any lot which falls out of specifications or demonstrates radical physical changes.
3. Stability data will be submitted as it becomes available.
4. (b) (4) was withdrawn as a supplier of the active ingredient in our correspondence of February 28, 1978.

A letter from (b) (4) authorizing us to refer to their Drug Master File number (b) (4) in support of our application is attached.

Sincerely yours,

CARTER-GLOGAU LABORATORIES DIVISION
CHROMALLOY PHARMACEUTICALS, INC.

Samuel M. Fainberg, Ph.D.
Director
Technical and Regulatory Affairs



JCW
encl

GENERAL OFFICES:
5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301
TELEPHONE (602) 939-7565 • TELEX 66-8304 (M-C LABS)

OCT 13 1978

NDA 85-825

Carter-Glogau Laboratories Division
Chromalloy Pharmaceuticals, Inc.
Attention: Dr. Samuel Fainberg
8160 West Bethany Home Road
Glendale, AZ 85301

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triamcinolone Acetonide Suspension, 40 mg. per ml.

We acknowledge receipt of your communication dated May 31, 1978.

We have completed the review of this abbreviated new drug application and have the following comments:

1.

(b) (4)

2.

3.

Please let us have your response promptly.

Sincerely yours,

cc:

LOS-DO DUP HFD-614

JMeyer/JTaylor

r/d/ init. JMeyer/MSeife 10-12-78

f/t/wlh/10-12-78

rev w/f

J. R. Bauglar
Marvin Seife, M.D.

Director

Division of Generic Drug Monographs

Office of Drug Monographs

Bureau of Drugs

JMeyer 10/12/78

10/13/78



CHROMALLOY PHARMACEUTICALS, INC.

A SUBSIDIARY OF CHROMALLOY AMERICAN CORPORATION

Orig

CARTER-GLOGAU LABORATORIES DIVISION

September 6, 1979

NOTED:
MEDICAL REVIEW INDICATED
SIG: *[Signature]*
DATE: *[Signature]*

RESUBMISSION

5/18/81 NDA ORIG AMENDMENT

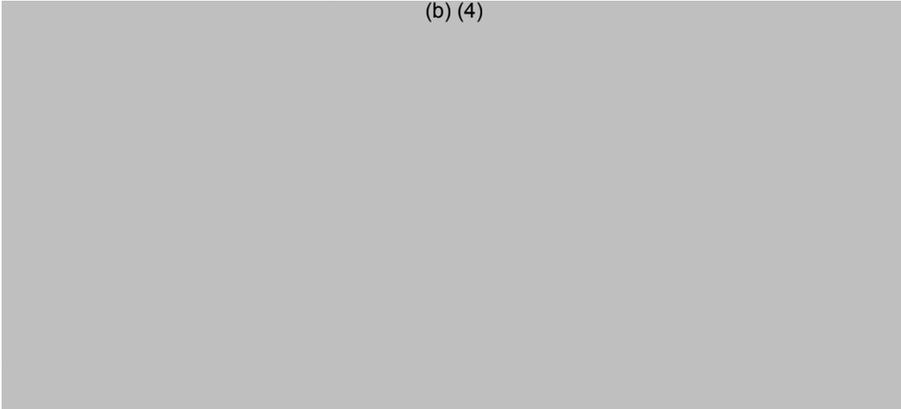
Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education,
and Welfare
Food and Drug Administration
Public Health Service
Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg
NDA 85-825

Dear Dr. Seife:

Reference is made to your letter of October 13, 1978 for Triamcinolone Acetonide Suspension.

We are supplying the following information, as requested.

1. (b) (4)

2. 

(Reports enclosed)



GENERAL OFFICES:
5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301
TELEPHONE (602) 939-7565 • TELEX 66-8304 (M-C LABS)

3.

(b)(4)

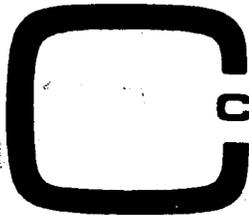
Sincerely yours,

CARTER-GLOGAU LABORATORIES DIVISION
CHROMALLOY PHARMACEUTICALS, INC

A handwritten signature in black ink, appearing to read "Samuel Fainberg", written over a horizontal line. The signature is cursive and somewhat stylized.

Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc
encls:



CARTER-GLOGAU LABORATORIES, INC.

Orig

September 20, 1979

NOTED
NO MEDICAL REVIEW INDICATED
SIG: _____
DATE: _____

5/18/80

ORIG NEW CORRES

Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education,
and Welfare
Food and Drug Administration
Public Health Service
Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg
NDA 85-825

Dear Dr. Seife:

We are attaching hereto FD Form 356H to amend our
NDA 850825 for Triamcinolone Acetonide Suspension.

Also attached is a copy of the letter executed by Mr.
Ronald M. Carter, President of Carter-Glogau Labora-
tories, Inc., which indicates the formal change of
name effective August 7, 1979.

There has been no change in the physical location of
the plant facilities in Glendale, Arizona, or Melrose
Park, Illinois. There is also no change in company
operations and personnel.

Changes in the signature lines on labeling will be
made at the next printing or within six months, whichever
ever date is first.

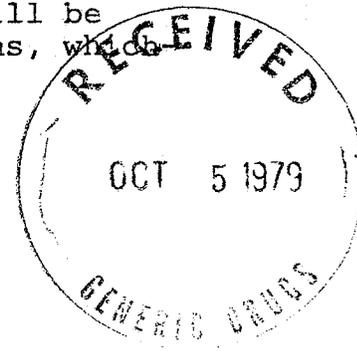
Sincerely yours,

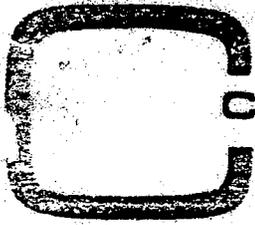
CARTER-GLOGAU LABORATORIES, INC

Samuel M. Fainberg

Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc





CARTER-GLOGAU LABORATORIES, INC.

Orig

RESUBMISSION

January 7, 1980

NOTED:
NO MEDICAL REVIEW INDICATED
SIG: _____
DATE: _____

NDA ORIG AMENDMENT

FPU

Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education,
and Welfare
Food and Drug Administration
Public Health Service
Rockville, MD 20857

118/81

**SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml
NDA 85-825**

Dear Dr. Seife:

We are attaching hereto FD Form 356H to supplement our NDA 85-825 for Triamcinolone Acetonide Suspension.

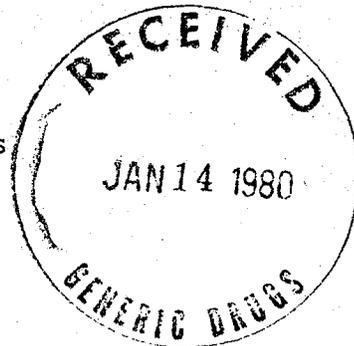
This supplement provides for the new labels, indicating the formal change of name and corporate structure, as per our commitment dated September 20, 1979.

Sincerely yours,

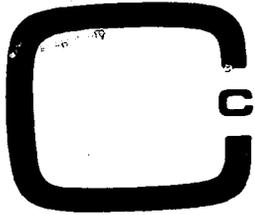
CARTER-GLOGAU LABORATORIES, INC

Samuel M. Fainberg

Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs



/edc
encls:



CARTER-GLOGAU LABORATORIES, INC.

Orig

September 25, 1980

Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education,
and Welfare
Food and Drug Administration
Public Health Service
Rockville, MD 20857

*PAI
ref
5/22/81
communication of
10/29/80 included
revised labeling that
was reviewed
EPL
MFO/REB*

NDA ORIG AMENDMENT

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml
NDA 85-825

Dear Dr. Seife:

We hereby supplement our NDA 85-825 for
Triamcinolone Acetonide Suspension.

This supplement provides for the revised package
insert in accord with the Glucocorticoid Guide-
lines of October, 1979.

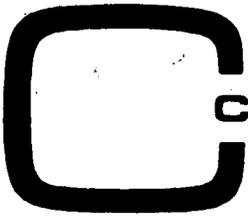
Sincerely yours,

CARTER-GLOGAU LABORATORIES, INC

Samuel M. Fainberg
Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc
encls:





CARTER-GLOGAU LABORATORIES, INC.

Orig

October 29, 1980

Marvin Seife, M. D.,
Director
Division of Generic Drug Monographs
HFD-530
Bureau of Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

ORIG NEW CORRES

EPL
OK
5/18/81

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40mg/ml
NDA 85-825

Dear Dr. Seife:

In reference to the insert revision format as per Federal Register Announcement, Vol. 45, No. 97, Friday, May 16, 1980, we are enclosing draft of insert revision for NDA 85-825 for Triamcinolone Acetonide Suspension, 40 mg/ml.

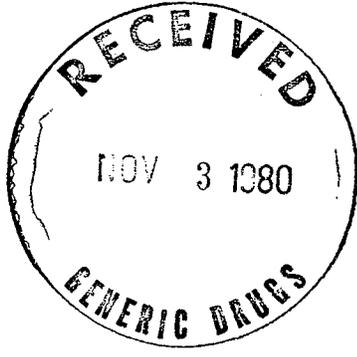
Your prompt review and approval of the draft insert will be greatly appreciated.

Sincerely yours,

CARTER-GLOGAU LABORATORIES, INC

Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc
encls:





CARTER-GLOGAU LABORATORIES, INC.

5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301 • TELEPHONE (602) 939-7565 • TELEX 66-8304

orig

March 18, 1981

ORIG NEW CORRES

Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education, and Welfare
Public Health Service
Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml
NDA 85-825

Dear Dr. Seife:

We hereby amend our NDA 85-825 for Triamcinolone Acetonide Suspension, 40 mg/ml.

This amendment provides for:

(b) (4)
[Redacted]

as alternate supplier of the active ingredient.

Drug Master File Referral from (b) (4) is enclosed.

There are no other changes and/or additions to this unapproved NDA.

Sincerely yours,

CARTER-GLOGAU LABORATORIES, INC

Samuel M. Fainberg

Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc
encls:





CARTER-GLOGAU LABORATORIES, INC.
 5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301 • TELEPHONE (602) 939-7565 • TELEX 66-8304

Dir

April 13, 1981

NDA ORIG AMENDMENT

Marvin Seife, M. D.
 Director
 Division of Generic Drug Monographs
 Office of Drug Monographs
 Bureau of Drugs
 Department of Health, Education, and Welfare
 Food and Drug Administration
 Public Health Service
 Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml.
 NDA 85-825

Dear Dr. Seife:

NOTED:
 NO MEDICAL REVIEW INDICATED
 SIG: *[Signature]*
 DATE: 5/18/81

We hereby amend our NDA 85-825 for Triamcinolone Acetonide Suspension.

This amendment provides for:

(b) (4)

as alternate supplier of the active ingredient.

Drug Master File Referral No. (b) (4) from (b) (4), is enclosed.

There are no other changes and/or additions to this unapproved NDA.

Sincerely yours,

CARTER-GLOGAU LABORATORIES, INC

[Signature]

Samuel M. Fainberg, Ph. D.
 Director
 Technical and Regulatory Affairs

/edc
 encls:



MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

TO : Division of Drug Manufacturing, HFD-320 DATE: 5/19/61
FROM : Division of Generic Drug Monographs, HFD- 530
Requester's Name: Robert C. Permisohn Phone: 34080
SUBJECT: GMP EVALUATION REQUEST

NDA, ANDA, and SUPPLEMENT NUMBER: FS-825

DRUG Trade Name: Triamcinolone Acetonide

DRUG Non-Proprietary Name: _____

DRUG CLASSIFICATION: A or B IC Other

PRODUCT CODE: SVP (description of dosage form, e.g.,
compressed tablet; coated tablet;
soft gelatin capsule; liquid; See Table)

180 DAY DATE: _____

APPLICANT'S NAME: Carter G. Loran Laboratories, Inc.

ADDRESS: 5160 West Bethany Home Road, Glendale,

FACILITIES TO BE EVALUATED: (Name, Address, and Responsibility)

① applicant



(b) (4)

Date Received: _____ Date Completed: _____

cc: HFD-320 (Orig)
HFD- (2 Copies)

MAY 22 1981

NDA 85-825

Carter-Glogau Laboratories, Inc.
Attention: Samuel M. Fainberg, Ph.D.
5160 West Bethany Home Road
Glendale, AZ 85301

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triamcinolone Acetonide Suspension, 40 mg./ml.

We acknowledge receipt of your communications dated September 6, 1979, September 20, 1979, January 7, 1980, October 29, 1980, and March 18, 1981, and April 13, 1981.

We have reviewed the submitted material and have the following comments:

1 a. The "How Supplied" section of the package insert labeling provides for 5 ml. and (b)(4) multi-dose containers. The January 7, 1980 communication included labeling for only the 5 ml. size containers. Clarify.

b. The package insert labeling should be revised to include the manufacturer of the subject drug product.

2. Particle size distribution specifications should be revised to be consistent with the particle size of the active ingredient raw material and the data submitted for the subject drug product.

3. It is recommended that a minimum of one new production lot manufactured each year be placed in the ongoing stability program.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 5/22/81
Marvin Seife, M.D.

Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs

5/21/81
J. Barzilai
R. Permissohn 5/21/81
J. Meyer 5/21/81

cc:
LOS-DO
HFD-616
RBarzilai/JLMeyer/RCPerrmissohn
R/D init JLMeyer/MSeife/5/20/81
pb/5/20/81
rev w/f
2623E



CARTER-GLOGAU LABORATORIES, INC.

5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301 • TELEPHONE (602) 939-7565 • TELEX 66-8304

Orig

June 4, 1981

NDA ORIG AMENDMENT

Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education, and Welfare
Public Health Service
Food and Drug Administration
Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml
NDA 85-825

Dear Dr. Seife:

Reference is made to your letter of May 22, 1981
for Triamcinolone Acetonide Suspension, 40 mg/ml.

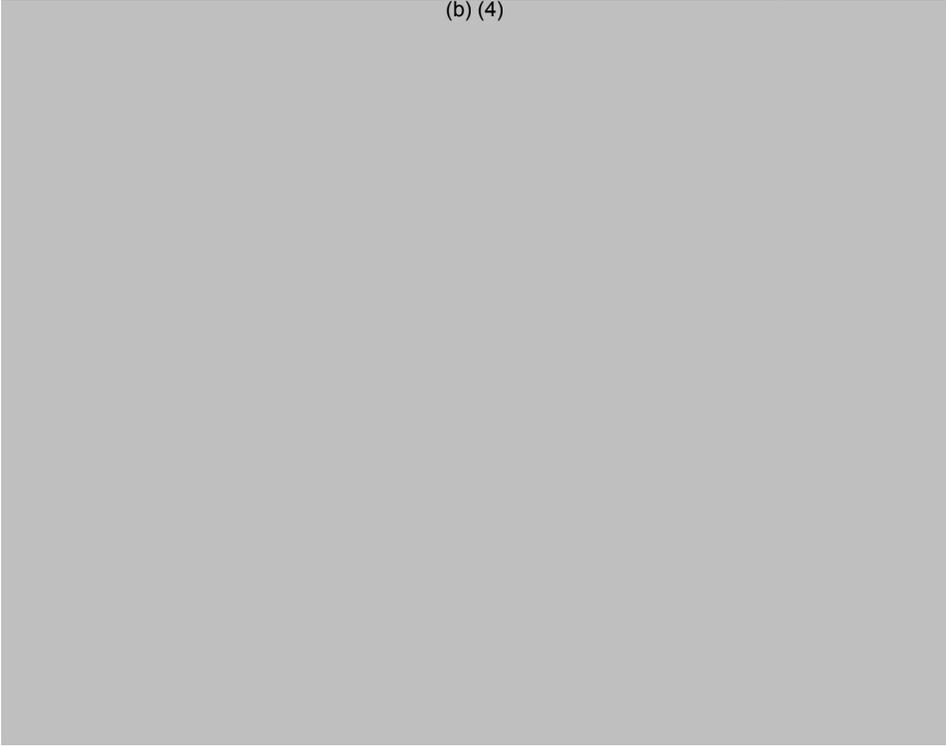
We are supplying the following information, as
requested.

- 1. a). We have revised our "How Supplied Section"
of the package insert (draft copies
enclosed) to include only the 5 ml. size
containers.
- b). We have added to the revised insert Carter-
Glogau Inc., Glendale, AZ 85301 as manufacturer
of the subject drug product.

2. (b) (4)

JUN 09 1981
GEN

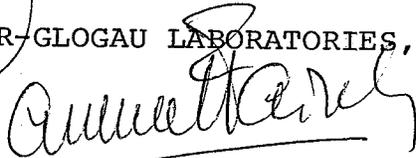
(b) (4)



3. We will place a minimum of one new product lot manufactured each year in the on-going stability program.

Sincerely yours,

CARTER-GLOGAU LABORATORIES, INC



Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc
encls:



CARTER-GLOGAU LABORATORIES, INC.

5160 WEST BETHANY HOME ROAD • GLENDALE, ARIZONA 85301 • TELEPHONE (602) 939-7565 • TELEX 66-8304

Orig

August 13, 1981

NDA ORIG AMENDMENT

Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Bureau of Drugs
Department of Health, Education,
and Welfare
Public Health Service
Food and Drug Administration
Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml
NDA 85-825

Dear Dr. Seife:

We hereby amend our NDA 85-825 for Triamcinolone
Acetonide Suspension.

This amendment provides for:

(b) (4)

as supplier of the active ingredient.

Drug Master File Referral No. (b) (4) from (b) (4)
is enclosed.

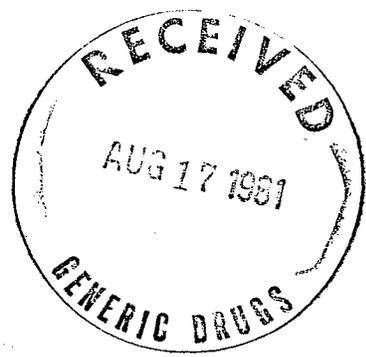
There are no other changes and or additions to
this unapproved NDA.

Sincerely yours,

CARTER-GLOGAU LABORATORIES, INC

Samuel M. Fainberg
Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc
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9/8/81
THE SUBMITTED TPL IS SATISFACTORY.
M.S.

August 20, 1981

NDA ORIG AMENDMENT

APPROVED EPL

Marvin Seife, M. D.
Director
Division of Generic Drug Monographs
Office of Drug Monographs
Bureau of Drugs
Department of Health, Education, and Welfare
Public Health Service
Food and Drug Administration
Rockville, MD 20857

SUBJECT: TRIAMCINOLONE ACETONIDE SUSPENSION, 40 mg/ml
NDA 85-825

Dear Dr. Seife:

In reference to our communication of June 4, 1981 for Triamcinolone Acetonide Suspension, 40 mg/ml., in response to your letter of May 22, 1981, we are enclosing final printed inserts.

Your prompt approval of the Abbreviated NDA will be greatly appreciated.

Sincerely yours,

CARTER-GLOGAU LABORATORIES, INC

Samuel M. Fainberg
Samuel M. Fainberg, Ph. D.
Director
Technical and Regulatory Affairs

/edc
encls:

