

Marketing New Drugs Evaluated in Drug Efficacy Study," published in the FEDERAL REGISTER July 14, 1970 (35 F.R. 11273).

A copy of the Academy's report has been furnished to the firm referred to above. Any other interested person may obtain a copy by request to the Food and Drug Administration, Press Relations Office (CE-200), 200 C Street SW., Washington, D.C. 20204.

Communications forwarded in response to this announcement should be identified with the reference number DESI 5595, 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 new drug applications: Office of
Scientific Evaluation (BD-100), Bureau of
Drugs.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-5), Bureau of Drugs.

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

Dated: May 20, 1971.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.71-8552 Filed 6-17-71; 8:45 am]

[DESI 5668]

CERTAIN COMBINATION GASTROINTESTINAL DRUGS

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 drugs:

1. Malglyn Tablets and Malglyn Compound Magma containing phenobarbital, belladonna alkaloids, and dihydroxyaluminum aminoacetate; Brayten Pharmaceutical Co., 1715 West 38th Street, Chattanooga, Tennessee 37409 (NDA 5-668).

2. Barbicaine Solution containing pentobarbital, phenobarbital, and procaine hydrochloride; Cutter Laboratories, Inc., 4th and Parker Streets, Berkeley, California 94710 (NDA 10-725).

3. Aludrox SA Suspension containing ambutonium bromide, butabarbital, aluminum hydroxide gel, and magnesium hydroxide; Wyeth Laboratories Div., American Home Products Corp., Post Office Box 8299, Philadelphia, Pa. 19101 (NDA 11-183).

4. Aludrox SA Tablets containing ambutonium bromide, butabarbital, dried aluminum hydroxide gel, and magnesium

hydroxide; Wyeth Laboratories (NDA 11-391).

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 reports, as well as other available evidence, and concludes that

1. Pentobarbital in combination with phenobarbital and procaine hydrochloride lacks substantial evidence of effectiveness for use as an adjunct in the treatment of organic diseases when accompanied by nausea and vomiting.

2. Aluminum hydroxide gel (or dried aluminum hydroxide gel) in combination with butabarbital, ambutonium bromide, and magnesium hydroxide lacks substantial evidence of effectiveness for use in the treatment of hypertrophic gastritis, diverticulitis of the colon, and postcholecystectomy syndrome.

3. The drugs listed in this announcement are possibly effective for their labeled indications other than those indications evaluated above.

B. *Marketing status.* 1. Within 60 days of the date of publication of this announcement in the FEDERAL REGISTER, the holder of any approved new drug application for a drug 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), describes in paragraphs (d), (e), and (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. Any other interested person may obtain a copy by request to the Food and Drug Administration, Press Relations Office (CE-200), 200 C. Street SW., Washington, D.C. 20204.

Communications forwarded in response to this announcement should be identified with the reference number DESI 5668, directed to the attention of the appropriate office listed below and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20852:

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

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

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-5), Bureau of Drugs.

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

Dated: May 24, 1971.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.71-8553 Filed 6-17-71; 8:45 am]

[DESI 8303]

HYDRALAZINE HYDROCHLORIDE

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 antihypertensive drugs:

Apresoline Hydrochloride Injection and Tablets containing hydralazine hydrochloride; Ciba Pharmaceutical Co., 556 Morris Avenue, Summit, N.J. 07901 (NDA 8-303).

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.

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

1. Hydralazine hydrochloride injection is (a) effective for the treatment of severe essential hypertension when the drug cannot be given orally or when there is an urgent need to lower blood pressure; and (b) probably effective for the treatment of hypertension associated with pre-eclampsic and eclampsic toxemia of pregnancy to prevent acute convulsant toxemia, and for the treatment of hypertension associated with acute glomerulonephritis when oral administration is inadvisable.

2. Hydralazine hydrochloride in tablet form is (a) effective for the treatment of essential hypertension; (b) probably

effective for the treatment of hypertension associated with acute glomerulonephritis; and (c) possibly effective for the treatment of hypertension associated with preeclampsia to prevent acute convulsant toxemia.

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.* Hydralazine hydrochloride preparations are in sterile aqueous solution form suitable for intramuscular or intravenous injection and in tablet form suitable for oral administration.

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. The labeling bears adequate information for safe and effective use of the drug and is in accord with the guidelines for uniform labeling published in the FEDERAL REGISTER of February 6, 1970. The "Indications" sections are as follows:

INDICATIONS

Hydralazine Hydrochloride Injection

For the treatment of severe essential hypertension when the drug cannot be given orally or when there is an urgent need to lower blood pressure.

For the treatment of hypertension associated with preeclamptic and eclamptic toxemia of pregnancy to prevent convulsant toxemia.

For the treatment of hypertension associated with acute glomerulonephritis when oral administration is inadvisable.

Hydralazine Hydrochloride Tablets

For the oral treatment of essential hypertension; may be used alone or as an adjunct. For the treatment of hypertension associated with acute glomerulonephritis.

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

a. 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 except for intravenous administration, adequate data to show the biologic availability of the drug in the formulation which is marketed, as described in paragraphs (a) (1) (i), (ii), and (iii) of the notice of July 14, 1970.

b. For any person who does not hold an approved or effective new drug application, the submission of an abbreviated new drug application, to include adequate data to assure the biologic availability of the drug in the formulation which is or is intended to be

marketed, as described in paragraph (a) (3) (ii) of that notice, except that bioavailability data are not required for intravenous administration of the drug.

c. 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.

d. 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), continued use as described in (c), (d), (e), and (f) of that notice.

Copies of the Academy's reports have been furnished to the firm referred to above. Any other interested person may obtain a copy by request to the Food and Drug Administration, Press Relations Office (CE-200), 200 C Street SW., Washington, D.C. 20204.

Communications forwarded in response to this announcement should be identified with the reference number DESI 8303, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20852:

Supplements (identify with NDA number):
Office of Scientific Evaluation (BD-100),
Bureau of Drugs, Original abbreviated new drug applications; (identify as such):
Drug Efficacy Study Implementation Project Office (BD-5), Bureau of Drugs.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-5), Bureau of Drugs.

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

Dated: May 21, 1971.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.71-8554 Filed 6-17-71; 8:45 am]

[DESI 6290; Docket No. FDC-D-324; NDA 5-845, etc.]

CERTAIN ANTIHISTAMINIC PREPARATIONS FOR ORAL OR RECTAL ADMINISTRATION

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 antihistaminic preparations for oral or rectal administration:

1. *Preparations containing bromodiphenhydramine hydrochloride.* a. Ambodryl Kapseals (NDA 7-984); and

b. Ambodryl Elixir (NDA 8-476); and
c. Ambodryl Syrup (NDA 8-745);
Parke, Davis & Co., Joseph Campau at the River, Detroit, Mich. 48232.

2. *Preparations containing chlorpheniramine maleate.* a. Chlor-Trimeton Tablets and Syrup (NDA 6-921); and

b. Chlor-Trimeton Repetabs Tablets (NDA 7-638); Schering Corp., 60 Orange Street, Bloomfield, N.J. 07003.

3. *Preparations containing cyproheptadine hydrochloride.* a. Periactin HCl Tablets (NDA 12-649); and

b. Periactin HCl Syrup (NDA 13-220); Merck Sharp & Dohme, Division Merck & Co., Inc., West Point, Pa. 19486.

4. *Preparations containing diphenhydramine hydrochloride.* a. Benadryl Syrup, Kapseals (capsules), Elixir, Emulets (enteric coated tablets), and Powder (for pharmaceutical dispensing purposes) (NDA 5-845); Parke, Davis & Co.

5. *Preparations containing diphenylpyraline hydrochloride.* a. Diafen Tablets (NDA 9-970); Riker Laboratories, 19901 Nordhoff Street, Northridge, Calif. 91326.

6. *Preparations containing promethazine hydrochloride.* a. Phenergan Tablets (NDA 7-935); and

b. Phenergan Syrup (NDA 8-381); and
c. Phenergan Rectal Suppositories (NDA 10-926 and NDA 11-689); Wyeth Laboratories Division, American Home Products Corp., Post Office Box 8299, Philadelphia, Pa. 19101.

7. *Preparation containing pheniramine maleate.* a. Trimeton Tablets (NDA 6-461); Schering Corp.

8. *Preparations containing pyrilamine maleate.* a. Neo-Antergan Maleate Tablets (NDA 6-290 and 7-119); Merck Sharp & Dohme.

9. *Preparations containing tripeleminamine hydrochloride or tripeleminamine citrate.* a. Pyribenzamine Tablets (NDA 5-914); Ciba Pharmaceuticals Co., Division of Ciba Corp., 556 Morris Avenue, Summit, N.J. 07901; and

b. Pyribenzamine Lontabs (sustained release tablet) (NDA 10-533); Ciba Pharmaceutical Co., Division of Ciba Corp.

c. Pyribenzamine Elixir (NDA 5-914); Ciba Pharmaceutical Co., Division of Ciba Corp.

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.

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

1. Bromodiphenhydramine Hydrochloride in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, allergic reactions to insect bites; physical

allergy; minor drug and serum reactions characterized by pruritus.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; motion sickness; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for migraine headache including allergic migraine; "histamine headache;" tissue preservative action; prevention or reduction of severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients; and "other conditions of a similar nature" (considered too broad to allow meaningful evaluation).

2. Chlorpheniramine Maleate in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for migraine headache including allergic migraine; "histamine headache;" tissue preservative action; prevention or reduction in severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients.

3. Cyproheptadine Hydrochloride in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; pruritus of chicken pox; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for: migraine headache including allergic migraine; "histamine headache;" tissue preservation action; prevention or reduction in severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients.

4. Diphenhydramine Hydrochloride in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus; intractable insomnia and insomnia predominant in certain medical disorders.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; use of desensitization procedures and when essential to use therapy known to be sensitizing; quieting the hyperactive emotionally disturbed child; prevention of postoperative nausea and vomiting; maintenance of normal sinus rhythm following recent conversion from atrial fibrillation; nausea and vomiting of early pregnancy; spasmolysis in gastrointestinal and other allergies characterized by smooth muscle spasm.

c. Lacking substantial evidence of effectiveness for migraine headache including allergic migraine; "histamine headache;" tissue preservation action,

prevention or reduction of severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients; antitussive action; Meniere's disease, nocturnal leg cramps, leg cramps of pregnancy, functional dysmenorrhea.

5. Diphenylpyraline Hydrochloride in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for: migraine headache including allergic migraine; "histamine headache;" tissue preservative action; prevention or reduction in severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients; nausea and vomiting of pregnancy.

6. Promethazine Hydrochloride in conventional oral or rectal dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus; intractable insomnia and insomnia predominant in certain medical disorders; prevention and control of the more severe, hazardous nausea and vomiting of pregnancy.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and

(other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for: migraine headache including allergic migraine; "histamine headache;" tissue preservative action; prevention or reduction in severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; nausea and vomiting of reflex origin; shortening of labor; prevention of allergic reactions to injection of allergenic substances; and "allergic conditions amenable to antihistamine therapy" (considered too broad to allow meaningful evaluation).

7. Pheniramine maleate in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus; prevention or relief of motion sickness.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for: migraine headache including allergic migraine; "histamine headache;" tissue preservative action; prevention or reduction in severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of the central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients; and "pheniramine maleate is of value clinically in the prevention and relief of many allergic manifestations" (considered too broad to allow meaningful evaluation).

8. Pyrilamine maleate in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus allergic dermatoses including contact dermatitis; relief of insect stings; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for: migraine headache including allergic migraine; "histamine headache;" tissue preservative action; prevention or reduction in severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients.

9. Tripeleminine Hydrochloride or Citrate in conventional oral dosage form is:

a. Effective or probably effective for the indications described in the "Indications" section which follows. The probably effective indications are: Mild, local allergic reactions to insect bites; physical allergy; minor drug and serum reactions characterized by pruritus.

b. Possibly effective for bronchial asthma; spasmodic bronchial cough; atopic dermatitis; neurodermatitis circumscripta; eczematoid dermatitis; allergic eczema; allergic dermatitis; contact dermatitis (including dermatitis venenata or poison ivy); chemotoxic dermatitis; generalized pruritus; pruritus ani and vulvae; secretory otitis media; prophylaxis of allergic reactions to contrast media; pruritus of jaundice; prophylaxis of penicillin and (other) drug reactions; pruritus of allergic dermatoses including contact dermatitis; relief of insect stings; use in desensitization procedures and when essential to use therapy known to be sensitizing.

c. Lacking substantial evidence of effectiveness for: migraine headache including allergic migraine; "histamine headache;" tissue preservative action; prevention or reduction in severity of sequelae of oral surgery (pain, trismus, edema, and hemorrhage); potentiation of the action of central nervous system depressants with resultant reduction of dosage of narcotic analgesics; prevention of allergic reactions to injection of allergenic substances; antiemetic effect in postoperative patients. The indication "many other "allergic conditions" is considered too broad to allow meaningful evaluation.

10. Chlorpheniramine Maleate and Tripeleminine Hydrochloride in sustained action dosage forms for oral administration are:

a. Probably effective for indications evaluated as effective and probably effective for conventional oral dosage forms of these drugs. (See paragraphs 2 and 9 above.)

b. Possibly effective and lacking substantial evidence of effectiveness for the same indications listed in these categories for the conventional oral dosage forms of these drugs in paragraphs 2 and 9 above.

B. Conditions for approval and marketing of drugs having an effective classification. 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. a. These preparations are in a conventional dosage form suitable for oral administration.

b. Diphenhydramine hydrochloride may also be in a powder form suitable for prescription compounding.

c. Promethazine hydrochloride may also be in a suppository form suitable for rectal administration.

2. Labeling conditions. a. The labels bear the statement, "Caution: Federal law prohibits dispensing without prescription."

b. Each drug is labeled to comply with all requirements of the Act and regulations. Its labeling bears adequate information for safe and effective use of the drug and is in accord with the guidelines for uniform labeling published in the FEDERAL REGISTER of February 6, 1970. The "Indications" section is as follows:

INDICATIONS

i. Bromodiphenhydramine Hydrochloride. Perennial and seasonal allergic rhinitis. Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug serum reactions characterized by pruritus.

ii. Chlorpheniramine Maleate. Perennial and seasonal allergic rhinitis. Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

iii. Cyproheptadine Hydrochloride. Perennial and seasonal allergic rhinitis. Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

iv. *Diphenhydramine Hydrochloride*.

Perennial and seasonal allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Parkinsonism (including drug-induced) in the elderly unable to tolerate more potent agents.

Mild cases of parkinsonism (including drug-induced) in other age groups.

In other cases of parkinsonism (including drug-induced) in combination with centrally acting anticholinergic agents.

Active and prophylactic treatment of motion sickness.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

Intractable insomnia and insomnia predominant in certain medical disorders.

v. *Diphenylpyrrolidine Hydrochloride*.

Perennial and seasonal allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

vi. *Promethazine Hydrochloride*.

Perennial and seasonal allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Preoperative, postoperative, or obstetric sedation.

Prevention and control of nausea and vomiting associated with certain types of anesthesia and surgery.

Therapy adjunctive to meperidine or other analgesics for control of postoperative pain.

Sedation in both children and adults as well as relief of apprehension and production of light sleep from which the patient can be easily aroused.

Active and prophylactic treatment of motion sickness.

Antiemetic effect in postoperative patients.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

Intractable insomnia and insomnia predominant in certain medical disorders.

Prevention and control of severe, hazardous nausea and vomiting of pregnancy.

vii. *Pheniramine Maleate*.

Perennial and seasonal allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

Prevention and relief of motion sickness.

viii. *Pyrilamine maleate*.

Perennial and seasonal allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Mild allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

ix. *Triphenylamine Hydrochloride and citrate*.

Perennial and seasonal allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

Dermographism.

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

Mild, local allergic reactions to insect bites.

Physical allergy.

Minor drug and serum reactions characterized by pruritus.

3. *Marketing status.* Marketing of such drugs may be continued under the conditions described in the notice entitled

"Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study," published in the FEDERAL REGISTER July 14, 1970 (35 F.R. 11273), as follows:

a. For holders of "deemed approved" new drug applications (i.e., an applica-

tion which became effective on the basis of safety prior to October 10, 1962), the submission of a supplement for revised labeling, an abbreviated supplement for updating information, and adequate data to show the biologic availability of the drug in the formulation which is marketed as described in paragraphs (a) (1) (i), (ii), and (iii) of the notice of July 14, 1970.

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

c. 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.

d. 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), continued use as described in (c), (d), (e), and (f) of that notice.

C. *Conditions for marketing drugs having no indication classified as effective.*

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 a drug which 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 and which contains an "Indications" section in accord with that described below. Such 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 delete such indications and to put the revised labeling into use within 60 days after the date of publication hereof in the FEDERAL REGISTER 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 to delete all claims for which substantial evidence of effectiveness is lacking as described in paragraph A above and to be in accord with this notice. Failure to delete such indications and to 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. Indications for which the drug is regarded as probably effective or possibly effective may continue to be used for 12 months or 6 months, respectively, following the date of this publication, to allow additional time within which holders of

previously approved applications or persons marketing the drug without approval may obtain and submit to the Food and Drug Administration data to provide substantial evidence of effectiveness, including evidence that the drug has the sustained action or prolonged effect claimed.

4. To be acceptable for consideration in support of the effectiveness of a drug, any such data must be previously unsubmitted, well organized, and include data from adequate and well controlled clinical investigations (identified for ready review) as described in § 130.12(a)(5) of the regulations published in the *FEDERAL REGISTER* of May 8, 1970 (35 F.R. 7250). Carefully conducted and documented clinical studies obtained under uncontrolled or partially controlled situations are not acceptable as a sole basis for the approval of claims of effectiveness, but such studies may be considered on their merits for corroborative support of efficacy and evidence of safety.

5. At the end of the 6-month and 12-month periods, any such data will be evaluated to determine whether there is substantial evidence of effectiveness of the drug for such uses. The conclusions concerning the drug will be published in the *FEDERAL REGISTER*. If no studies have been undertaken or if the studies do not provide substantial evidence of effectiveness, procedures will be initiated to withdraw approval of the new drug application for the drug, pursuant to the provisions of section 505(e) of the Federal Food, Drug, and Cosmetic Act. Withdrawal of approval of the application will cause any such drug on the market to be a new drug for which an approval is not in effect.

6. Labeling revised pursuant to this notice should take into account the comments of the Academy, furnish adequate information for safe and effective use of the drug, be in accord with the guidelines for uniform labeling (§ 3.74) published in the *FEDERAL REGISTER* of February 6, 1970, and recommend use of the drug (for the probably effective indications) as follows: (The possibly effective indications may also be included for 6 months).

INDICATIONS

(The "Indications" sections are the same as those listed for the conventional dosage forms of chlorpheniramine maleate and tripeleminamine hydrochloride in paragraph B.2 above.)

D. *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 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. Promulgation of the proposed order would cause any re-

lated drug for human use offered for the indications for which substantial evidence of effectiveness is lacking to be a new drug for which an approved new drug application is not in effect. Any such drug then on the market would be subject to regulatory proceedings.

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

3. A request for a hearing may not rest upon mere allegations or denials but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing, together with a well organized and full factual analysis of the clinical and other investigation 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 § 130.12(a)(5) of the regulations published in the *FEDERAL REGISTER* of May 8, 1970 (35 F.R. 7250). Carefully conducted and documented clinical studies obtained under uncontrolled 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.

A copy of the Academy's report has been furnished to each firm referred to above. Any other interested person may obtain a copy by request to the appropriate office named below.

Communications forwarded in response to this announcement should be identified with the reference number DESI 6290, directed to the attention of the following appropriate office, and addressed (unless otherwise specified), 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 application (Identify as such): Drug Efficacy Study Implementation Project Office (BD-5),
Bureau of Drugs.

Request for hearing (Identify with Docket number): Hearing Clerk, Office of General Counsel (GC-1), Room 6-62, Parklawn Building.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-5), Bureau of Drugs.

Requests for NAS-NRC report: Press Relations Office (CE-200), Food and Drug Administration, 200 C Street SW., Washington, D.C. 20204.

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

Dated: May 17, 1971.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc. 71-8557 Filed 6-17-71; 8:46 am]

[DESI 8692]

THYROTROPIN FOR INJECTION

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 thyroid stimulating hormone drug for injectable use:

Thyrotropin (thyrotropin) Sterile Lyophilized Powder; Armour Pharmaceutical Co., Box 1022, Chicago, Ill. 60690 (NDA 8-682).

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. A new drug application is required from any person marketing such drug without approval.

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

1. Thyrotropin is effective for use in determining subclinical hypothyroidism or low thyroid reserve; to differentiate primary and secondary hypothyroidism; to evaluate the need for thyroid medication in patients already receiving thyroid therapy; for treatment of functioning thyroid carcinoma; and to aid in detection of remnants and metastases of thyroid carcinoma.

2. Thyrotropin is probably effective in differentiating diagnosis of Hashimoto's thyroiditis or struma lymphomatosa (primary thyroid failure with compensatory enlargement) from nontoxic adenomatous goiter.

3. Thyrotropin is possibly effective in the treatment of toxic adenomatous goiters and in counteracting the effects of Lugol's solution.

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.* Thyrotropin preparations are in sterile lyophilized powder