

[DESI 10598]

**ANTIEMETIC COMBINATION
PREPARATION****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 Bendectin Tablets containing dicyclomine hydrochloride, doxylamine succinate, and pyridoxine hydrochloride; Merrell-National Laboratories, Division of Richardson-Merrell, Inc., 110 East Amity Road, Cincinnati, Ohio 45215 (NDA 10-598).

This drug is regarded as a new drug (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 this preparation is possibly effective for nausea and vomiting of pregnancy.

B. Marketing status. Marketing of such drug with labeling which recommends or suggests its use for indications for which it has been classified as possibly effective may be continued for six months as described in paragraphs (d), (e), and (f) of the notice Conditions for 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. Communications forwarded in response to this announcement should be identified with the reference number DESI 10598, 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.

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

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

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

Dated: June 27, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-10455 Filed 7-7-72;8:48 am]

[DESI 12152]

**CERTAIN ANTIHISTAMINE-CON-
TAINING DRUG CONTAINING
CHLORPHENIRAMINE MALEATE,
PHENYLPROPANOLAMINE HYDRO-
CHLORIDE, AND ISOPROPAMIDE
IODIDE****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 for oral use:

Ornade Spansules (sustained release capsules) containing chlorpheniramine maleate, phenylpropanolamine hydrochloride, and isopropamide iodide; Smith, Kline & French Laboratories, 1500 Spring Garden Street, Philadelphia, Pa. 19101 (NDA 12-152).

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:

1. This drug is possibly effective for relief of upper respiratory tract congestion and hypersecretion associated with vasomotor rhinitis and allergic rhinitis, and for prolonged effect.

2. The drug lacks substantial evidence of effectiveness for relief of nasal congestion and hypersecretion associated with: the common cold; sinusitis (acute, subacute and chronic); influenza; and postnasal drip.

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 which a drug is classified in paragraph A. 2. 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. 2. above. Failure to delete such indications and put the revised labeling into use within 60

ditions 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 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. Clinical trials which have established effectiveness of the drug may also serve to establish the bioavailability of the drug if such trials were conducted on the currently marketed formulation.

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 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.

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 12462, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20852:

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

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

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

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

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

Dated: June 27, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-10457 Filed 7-7-72;8:48 am]

NOTICES

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. Communications forwarded in response to this announcement should be identified with the reference number DESI 12152, 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.

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

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

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

Dated: June 27, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-10456 Filed 7-7-72;8:48 am]

[DESI 4084]

CERTAIN OTC BRONCHODILATORS AND ANTI-ASTHMATIC PREPARATIONS

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has received reports from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, for the over-the-counter drugs listed below. Pending the results of the OTC study of drugs in this class, action on these reports will be deferred in accordance with the proposal published in the FEDERAL REGISTER of April 20, 1972 (37 F.R. 7807) entitled "Over-the-Counter Drugs" concerning the status of drugs previously reviewed under the Drug Efficacy Study.

The following OTC bronchodilators and antiasthmatic drugs are included in this announcement:

1. Enofen Tablets containing phenobarbital, theophylline, and ephedrine sulfate; Kremers-Urban Co., 5600 West County Line Road, Mequon, Wis. 53201 (NDA 4-084).

2. Tedral and Tedral Half Strength Enteric Coated Tablets containing phenobarbital, theophylline, and ephedrine hydrochloride; Warner-Chilcott Laboratories, Div. Warner-Lambert Pharmaceutical Co., 201 Tabor Road, Morris Plains, N.J. 07950 (NDA 4-508).

The evaluations of the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, Panel on Drugs Used in Allergy, and Panel on Drugs Used in Respiratory Disturbances are as follows:

1. Enofen tablets containing phenobarbital, theophylline, and ephedrine sulfate.

PANEL ON DRUGS USED IN ALLERGY

Indication: Bronchial asthma.

Evaluation: Effective, but * * *

Comments: Oral ephedrine in 25-mg. dosage is an effective drug in bronchial asthma, and phenobarbital is a useful additive to counteract the excitatory effects of ephedrine. Oral theophylline in the hydrous form, however, is absorbed irregularly, and is of doubtful value in this combination. Although there is no direct available published evidence on blood levels after oral theophylline (hydrous), it seems unlikely, by analogy with other theophylline compounds, that this dose will produce therapeutically useful blood levels of theophylline.

This indication was reevaluated as possibly effective with the following additional comment:

However, in view of recent evidence that the inhibitory effect of theophylline on phosphodiesterase may supplement the adenylyl cyclase-stimulating action of sympathomimetics in inhibiting mediator release in immediate hypersensitivity, it is possible that the theophylline could act synergistically with ephedrine at dosage levels not in themselves effective. However, this has not been shown clinically.

General comments: The insert should warn that some patients develop acute urinary retention as a side effect of ephedrine. This occurs most commonly in men with prostatic hypertrophy, but it has been reported to occur in some women as well.

PANEL ON DRUGS USED IN RESPIRATORY DISTURBANCES

Indication: Bronchial asthma.

Evaluation: Effective, but * * * (Subsequently reevaluated as possibly effective.)

Comments: There is no evidence that this product is more effective than ephedrine alone. Theophylline is probably ineffective at the dosage suggested.

The Panel objects to the inclusion of phenobarbital in this product. If sedation is necessary in the management of a patient with severe asthma or emphysema, it should be given independently of other medications so that the effects and side effects of each can be individually controlled. However, combinations of ephedrine and phenobarbital are often useful in patients with mild episodic asthma.

2. Tedral and Tedral Half Strength Enteric Coated Tablets containing phenobarbital, theophylline, and ephedrine hydrochloride.

PANEL ON DRUGS USED IN ALLERGY

Indication: Bronchial asthma.

Evaluation: Possibly effective.

Comments: Oral ephedrine in 25-mg. dosage is an effective drug in bronchial asthma, and phenobarbital is a useful additive to counteract the excitatory effects of ephedrine. Oral theophylline (hydrous) is absorbed irregularly, and is of doubtful value in this combination. The properties of en-

teric coating are not well documented, and if delayed absorption results from the enteric coating, effective levels of ephedrine may not be attained.

Indication: Hay fever.

Evaluation: Possibly effective.

Comments: The Panel fails to discern the rationale for giving theophylline in hay fever.

PANEL ON DRUGS USED IN RESPIRATORY DISTURBANCES

Indication: Bronchial asthma.

Evaluation: Possibly effective.

Comments: The properties of this specific product have not been defined. Because of the enteric coating of this product, suitable clinical studies must be done to establish its efficacy. If absorption of the ingredients is not hindered, the effectiveness of the product would be due to the ephedrine, because oral theophylline is probably ineffective at the dosage suggested.

The Panel objects to the inclusion of phenobarbital in this product when it is used in patients with severe asthma. If sedation is necessary in the management of a patient with asthma, it should be given independently of other medications so that the effects and side effects of each can be individually controlled. However, combinations of ephedrine and phenobarbital are often useful in patients with mild episodic asthma.

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 4084, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20852:

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. 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: April 28, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-14050 Filed 7-7-72;8:47 am]

[DESI 1205]

CERTAIN OTC COLD REMEDIES Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has received reports from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, for the over-the-counter drugs listed below. The Academy's reports constitute an important element of the totality of information considered by the Administration in reaching its conclusions concerning the effectiveness of drugs in the Drug Efficacy Study and the marketing