EVALUATION: Effective, but * * *

Comments: This combination contains the known analgesic, aspirin, which at the recommended dose would provide relief of pain. There is no reason to expect that the additional ingredients would detract from or add to this effect.

This combination is probably capable of relieving many different kinds of pain. However, there are no specific well controlled, conclusive studies on the above-mentioned conditions.

INDICATION: For minor muscle aches and pains resulting from fatigue, overexertion, or exposure.

EVALUATION: Effective, but * * *

Comments: This combination contains the known analgesic, aspirin, which as stated in the first two indications would provide relief of pain. The panel, however, objects to vague and ill-defined conditions such as "fatigue, overexertion, and exposure," which may not be associated with pain. It would be better to delete these conditions.

GENERAL COMMENTS: Whether the addition of phenyltoloxamine and glyceryl guaiacolate contributes anything to the management of the clinical entities "neuralgia, arthritis, rheumatism" is not known.

The drug is advertised as a "new and different analgesic for more pain relief" and contains in addition to aspirin an anti-inflammatory agent. The panel considered the claim "new and different pain relief" and in that there is no valid evidence of "more pain relief" and the drug is not "new" or "different.

Under "What you can expect of Defencin," the statement is made: "Clinical studies have shown that most patients who use Defencin have experienced relief of pain." Among the remainder, the principal side effects were minor stomach irritation similar to those from aspirin alone. This may be true, but also glyceryl guaiacolate may cause stomach irritation.

Two tablets every 3 or 4 hours are recommended. This means 25 mg. phenyltoloxamine every 3 hours, i.e., presumably enough to cause dryness. In the light of this side effect, the panel objects to the other statements made by the company: "Defencin has been found to be sufficiently free of undesirable side effects—so safe—that it is sold without prescription. In fact, because Defencin is safe, you can use it repeatedly."

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

GENERAL COMMENTS: The Panel on Drugs Used in Rheumatic Diseases recommends that certain vague and ill-defined claims be modified or deleted. The following is a list of these claims.

1. Lumbago, stiffness, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic, and arthritis.

The claims in the first category are of such different etiologies that it would be better to specify the diseases (e.g., osteoarthritis, rheumatoid arthritis, and arthrosis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientific terms which are undefined in the Panel and should be deleted. Because these claims are vague and ill-defined, the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

PANEL ON NEUROLOGICAL DRUGS

GENERAL COMMENTS: The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuritis, neuritis, and radiculitis because of the multiple known and unknown etiological conditions. Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots and are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis should be deleted from brochures and package inserts.

PANEL ON DRUGS IN ALLEGORY

INDICATION: Relief of common cold symptoms, such as runny nose and sneezing.

EVALUATION: Possibly effective.

Comments: Phenyltoloxamine, in the experience of the panel, is only weakly active as an antihistamine. There are no carefully controlled studies, in which different antihistamines were tried, disclosed no alleviation of symptoms or shortening of the duration of symptoms of colds. When allergic rhinitis is mistaken for a cold, antihistamines may be of benefit; but allergic rhinitis is being treated in that instance, not an upper respiratory infection.

This indication was subsequently reevaluated as ineffective as a fixed combination with the following additional comments:

The evidence presented by the manufacturers of Defencin is not adequate to support the efficacy of this combination. The major category of controlled studies to support the use of Defencin as a sedative was not documented.

The studies purporting to demonstrate that phenyltoloxamine improved the action of aspirin through its sedative effect was not convincing; although by inference with other studies, this might be the case. It has not been proven that the antihistamine contributes to the relief of cold symptoms which is the primary effect of this combination.

The majority of carefully controlled studies that have been performed with antihistamines disclosed no alleviation of symptoms, or shortening of the duration of symptoms of colds. When allergic rhinitis is mistaken for a cold, antihistamines may be of benefit, but allergic rhinitis is being treated in that instance, not an upper respiratory infection.

INDICATION: Relief of cough.

EVALUATION: Effective, but * * *. Subsequently reevaluated as ineffective as a fixed combination.

Comments: Glyceryl guaiacolate is an effective expectorant that is helpful in relieving nonproductive coughs. There is no evidence that the antihistamine or aspirin contributed significantly to this effect.

A copy of the Academy's report has been furnished to each firm referred to above. Comments in response to this announcement should be identified with the reference number DESI 6499, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 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-69), Bureau of Drugs.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 503, 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).


SAM D. FINE, Associate Commissioner for Compliance.

[FR Doc. 79-5978 Filed 4-19-72; 8:47 am]

CERTAIN OTC ANTACID 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 "Proposed Establishing Status of Over-the-Counter Drugs Previously Reviewed Under the Drug Efficacy Study (DESI)" published elsewhere in this issue of the Federal Register.

The following OTC antacid drugs are included in this announcement.

1. Chooz Chewing Gum Tablets containing calcium carbonate and magnesium stearate; Philco-Chimbac, Galloping Hill Rd, Kenilworth, N.J. 07033 (NDA 1-375).

2. Kamat Tablets containing aspirin, aluminum hydroxide, magnesium trisilicate, and kaolin; Ciba Pharmaceutical Co., Inc., 3715-31 Laedle Ave., St. Louis, Mo. 63101 (NDA 1-652).


6. Gelusil Tablets containing magnesium trisilicate and aluminum hydroxide; Warner-Chilcott Laboratories (NDA 4-360).

7. Algin Tablets and Alginan Magma containing dihydroxyaluminum aminoatellate; Braxton Pharmaceuticals Co., 1715 West 38th Street, Chattanooga, Tenn. 37409 (NDA 5-660).

8. Alzinox Tablets and Alzinan Magma containing dihydroxyaluminum aminoatellate; Smith, Miller & Patch, Inc., 401 Joyce Kilmer Avenue, New Brunswick, N.J. 08902 (NDA 5-647).

9. Carmethox Suspension containing sodium carboxymethylcellulose; and Magnesite Tablets containing sodium carboxymethylcellulose and magnesium oxide; Ciba Pharmaceutical Co., Division of Ciba Corp., 588 Morris Avenue, Summit, N.J. 07901 (NDA 5-738).

10. Carmethose-Traesite Tablets containing sodium carboxymethylcellulose, adiphene hydrochloride, and magnesium oxide; Ciba Pharmaceutical Co., Division of Ciba Corp., 588 Morris Avenue, Summit, N.J. 07901 (NDA 6-738).

11. Resinafit Capsules and Tablets containing ployaminemethylene resin; Merrell-National Drug Co., Division of
13. Kelonty Tablets containing dicyclomine hydrochloride, aluminum hydroxide, magnesium carbonate, and methylcellulose; Merrell-National Drug Co. (NDA 7-911).
15. Kolcryst Gel containing dicyclomine hydrochloride, aluminum hydroxide, magnesium hydroxide, and methylcellulose; Merrell-National Drug Co. (NDA 7-911).

The evaluations of the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, are as follows:

1. Choos Chewing Gum Tablets containing calcium carbonate and magnesium trisilicate.
This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: Fast relief of heartburn.
Evaluation: Probably effective.
Comments: The ingredients in this preparation are useful in this regard when belching is associated with gastroesophageal reflux of acid gastric contents.

2. Gelusil Tablets containing aluminum carbonate, magnesium carbonate, and calcium carbonate; Merrell-National Drug Co. (NDA 9-116).
This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: For the temporary relief of gastric hyperacidity.
Evaluation: Probably effective.
Comments: In the dosage advocated, the amount of atropine (0.260 mg.) does not increase the amount of air swallowed.

3. Amphojel Tablets containing aluminum hydroxide.
This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: As an antacid.
Evaluation: Effectively.
Comments: Amphojel is representative of a large group of aluminum hydroxide preparations. While the label states that Hemet has any effect on gastric hyperacidity, there is no evidence supporting the claim that the presence of hyperacidity has not been established; neither has the presence of gastritis. The sodium concentration of the antacid should also be stated.

4. Gelusil Liquid containing magnesium trisilicate and aluminum hydroxide.
This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: For acid control in gastritis and hyperacidity.
Evaluation: Probably effective.
Comments: The ingredients contained in this drug, aluminum hydroxide and magnesium trisilicate have been shown to adsorb pepsin and in this way inhibit peptic activity. Whether adsorption of toxic gases, bacteria, histamine, etc., in the gastrointestinal tract is clinically significant is unproven.

5. Endo-Magnal Suspension containing magnesium trisilicate and aluminum hydroxide.

This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: Antacid.
Evaluation: Effective.
Comments: The ingredients in this drug (magnesium trisilicate and aluminum hydroxide) have been found to increase the 

6. Gelusil Tablets containing magnesium trisilicate and aluminum hydroxide.
This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: As an antacid.
Evaluation: Possibly effective.
Comments: Both ingredients adsorb in vitro but whether adsorption of toxins, gases, bacteria, histamine, etc., is significant is unproven.

7. Algin Tablets and Algin Magma containing dihydroxy aluminum aminoacetate.

These drugs have been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: For acid control in gastritis and hyperacidity.
Evaluation: Probably effective.
Comments: Both ingredients adsorb in vitro. Algin Magma has been shown to adsorb pepsin and in this way inhibit peptic activity. Whether adsorption of toxic gases, bacteria, etc., is significant is unproven.

8. Alinex Tablets and Alinex Magma containing dihydroxyaluminum aminoacetate.

These drugs have been evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: "As an antacid for the relief of gastric hyperacidity * * *
Evaluation: Possibly effective.
Comments: Gastric hyperacidity is not a clinical entity and there is no known relation between the gastric acid level and symptoms. The presence of a given level of gastric acidity does not call for therapy.
Indication: "For physicians' use in the management of peptic ulcer patients."
Evaluation: Effective.
Comments: The package labels make no claim and Alloidox and Alloidox Magne are tablet and suspension respectively, of dihydroxyaluminum aminoacetate. These compounds are antacids whose activity is comparable with that of aluminum hydroxide.

9. Carmethose Suspension containing sodium carboxymethylcellulose;
10. Carmethose with Magnesium Oxide Tablets containing sodium carboxymethylcellulose and magnesium oxide;
11. Carmethose-Trasentine Tablets containing sodium carboxymethylcellulose, adphenine hydrochloride, and magnesium oxide.

These drugs were evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: "For the temporary relief of gastrointestinal discomfort due to hyperacidity."
Evaluation: Possibly effective.
Comments: Carboxymethylcellulose is a weak antacid, with a very low neutralizing capability. The magnesium oxide combined with Carmethose probably provides the important neutralizing capacity of this combination. More evidence is needed to demonstrate that the carboxymethylcellulose makes a significant addition.

Furthemore, the indication of "gastro discomfort due to hyperacidity" is highly dubious, in that there is no consistent relationship between the level of gastric acidity and symptoms.

The addition of Trasentine to Carmethose in no way changes the evaluation of this preparation.

12. Rednat capsules and tablets containing polyaminemethylenic resin.

These drugs were evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: "Effective for the temporary relief of gastric hyperacidity."
Evaluation: Probably effective.
Comments: Rednat has been shown to have antacid action, but its clinical efficacy in relieving symptoms induced by acid has not been compared with other standard products.

General comments. The tonic form of the resin should be stated. If the resin contains sodium, potassium, or ammonium the amount per tablet should be stated.


This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: "Fast temporary relief of acid digestion or heartburn due to gastric hyperacidity."
Evaluation: Possibly effective.


This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: "Excess stomach acidity."
Evaluation: Probably effective.
Comments: The label implies that the preparation is effective from "the effects of excess stomach acidity"; hyperacidity is a laboratory finding, not a clinical entity.

Indication: Heartburn.
Evaluation: Probably effective.
Comments: The different antacid components of this preparation have been shown to neutralize HCl. Similar preparations with the same ingredients as Dimacid B or combinations thereof have been shown to alleviate the symptom heartburn.
Indication: Gas.
Evaluation: Possibly effective.
Comments: There is no evidence supporting the claim that aerophage symptoms can be relieved by any of the ingredients in this preparation.

Indication: "Upset or sour stomach."
Evaluation: Possibly effective.
Comments: The term used in this indication is very vague. The symptoms attributed to the patient or sour stomach may be due to a variety of conditions, some pertaining to the gastrointestinal tract (duodenal ulcers, etc.), and some originating in other organs (postprandial angina, etc.).
General comments. This preparation has no package insert and the information on the label is inadequate, as far as side effects and contraindications are concerned. The dose recommended is two tablets when needed. The presence of aluminum carbonate in this preparation makes it imperative to establish a dosage schedule, with a warning about the possible danger of high doses for a long period due to the inherent danger of milk-alkali syndromes, renal stones, etc., as well as the advisability of assessing the serum level of calcium before and during the treatment (function, etc.). The statement that Dimacid B does not cause "acid rebound or harmful overalkalinizing" has not been substantiated.

15. Kolanpty Gel containing dicyclomine hydrochloride, aluminum hydroxide, magnesium hydroxide, and methylcellulose.

This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: "Temporary relief of acid indigestion or heartburn due to gastric hyperacidity."
Evaluation: Possibly effective.


This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: Heartburn, gas, indigestion, and upset or sour stomach due to excessive gastric acid.
Evaluation: Probably effective.
Comments: The warnings and dose schedule are inadequate.

General comments. This preparation has no package insert and the information on the label is inadequate, as far as side effects and contraindications are concerned. The dose schedule is limited to: "chew 1 or 2 tablets as required."

17. Rolaid Antacid Mint with HMAS Tablets containing almidrate sulfate.

This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: Heartburn, gas, indigestion, and upset or sour stomach due to excessive gastric acid.
Evaluation: Probably effective.
Comments: No clinical data are available to the Panel, inasmuch as all the references are proprietary. However, the relief of such symptoms by other alkaline medication has often been demonstrated and apparently will provide adequate amounts of this compound. However, this compound has not been adequately tested.

General comments. This preparation has no package insert and the information on the label is inadequate, as far as side effects and contraindications are concerned. The dose schedule is limited to: "chew 1 or 2 tablets as required."

18. A-Plus Tablets containing isomylamine HCl, calcium carbonate, magnesium carbonate, and magnesium trisilicate.

This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.
Indication: Neutralizes excess acid.
Evaluation: Probably effective.
Comments: This indication as stated is proper if a sufficient dose of the compound is taken and if the condition of "excess acidity" can be recognized by the consumer. The dosage should be chewed thoroughly for maximum benefit.

Indication: Relaxes nervous stomach.
Evaluation: Possibly effective.
NOTICES

[DESI 5213]

CERTAIN COUGH PREPARATIONS

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:


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 these drugs are probably effective for the temporary relief of cough.

B. Marketing status.

1. Marketing of such drug with labeling which recommends or suggests its use for indications for which it has been classified as probably effective may be continued for 12 months as described in paragraphs (e), (f), and (g) of the notice “Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study” published in the Federal Register July 14, 1970 (55 F.R. 11273).

2. Within 60 days from publication hereof in the Federal Register, the holder of any approved new drug applications for such drug is requested to submit a supplement to his application to provide for revised labeling as needed, which, taking into account the comments of the Academy, furnishes adequate information for safe and effective use of the drug; is in accord with the guidelines for uniform labeling published in the Federal Register, February 8, 1970 (21 CFR 3.74); and recommends use of the drug for the probably effective indication as follows:

INDICATION

SYMPTOMATIC RELIEF OF COUGH

The supplement should be submitted under the provisions of 139.9 (d) and (e) of the new drug regulations (21 CFR 139.9 (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.

3. After 60 days following publication hereof in the Federal Register, any such drug on the market without an approved new drug application and shipped within the jurisdiction of the Food, Drug, and Cosmetic Act should be labeled in accord with this notice.

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 5213, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5000 Fishers Lane, Rockville, Md. 20852.

Supplements (identify with NDA number):
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 should be directed to the Food and Drug Administration, 5000 Fishers Lane, Rockville, Maryland 20852.

Requests for the Academy’s report:
Drug Efficacy Study Information Control (BD-67), 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).


SAM D. FINE,
Associate Commissioner for Compliance.

[DESI 7387]

DRUGS CONTAINING OXYCODONE HYDROCHLORIDE, OXYCODONE TEREPHTHALATE, HOMATROPINE TEREPHTHALATE, ASPIRIN, PHENACETIN, AND CAFFEINE; OXYCODONE HYDROCHLORIDE, OXYCODONE TEREPHTHALATE, HOMATROPINE TEREPHTHALATE, AND PENTYLENETETRAZOL; OR MEPERIDINE HYDROCHLORIDE AND PRO-METHAZINE 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 drugs:

1. Percodan Tablets containing oxy-
codone hydrochloride, oxycodone tereph-
thalate, homatropine terephthalate, aspirin, phenacetin, and caffeine; Endo Laboratories, Inc., 1000 Stewart Avenue, Garden City, Long Island, N.Y. 11550 (NDA 7–335).

2. Nucodan Tablets containing oxy-
codone hydrochloride, oxycodone tereph-
thalate, homatropine terephthalate, and promethazine; Endo Laboratories, Inc. (NDA 7–337).

3. Mepergan Capsules and Mepergan Fortis Capsules containing meperidine hydrochloride and promethazine hydro-
dride; Wyeth Laboratories, Inc., Post Office Box 9299, Philadelphia, Pa. 19101 (NDA 11–730; see below).

Such drugs are regarded as new drugs (21 U.S.C. 321(p)). The effectiveness...