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Indication: Bronchial asthma.
Evaluation: Effective, but...
Comments: Oral ephedrine in 25-mg. dosage is an effective drug in bronchial asthma, and it is helpful 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 likely that, analogous to theophylline and other theophylline compounds, that this dose will produce aapeutically 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 adenylcyclase-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 more 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...
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.


SAMI D. FINE,
Associate Commissioner for Compliance.

[DESI 2086]

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. Pending the results of this 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 4-804).

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-
It is recognized that although the over-the-counter drug products reviewed by the Academy are relatively few in number, they are representative of many such preparations on the market—products which are identical, similar, or related, and competitive. Although some of the other marketed articles differ qualitatively and/or quantitatively and some bear drug claims differing from those reviewed by the Academy, they generally contain ingredients which are of the same pharmacologic class as those reviewed by the Academy. Therefore, conclusions reached by the Academy about the drugs they reviewed are applicable to related or identical drugs not under review, and the Academy’s ratings may be applicable as well.

It is recognized that new evidence of effectiveness may have become available since this publication was submitted to the Academy for review. It is also recognized that for many drugs substantial evidence in support of at least some of their recommended uses is not available.

The need for review of all over-the-counter drugs by the Food and Drug Administration with the assistance of advisory committees was announced in the Federal Register, May 11, 1972. The establishment of a consistent policy for each class of OTC drugs and to ensure equitable treatment of all firms marketing competitively over-the-counter drugs is further implementation of the Drug Efficacy Study (DES) program as it pertains to the OTC drugs listed here and related OTC drugs is deferred pending the results of the OTC study. (See “Over-the-Counter Drug Products Reviewed under the Drug Efficacy Study.”) The Academy is not in a position to make available to interested persons the opinions of the Drug Efficacy Study Group of the National Academy of Sciences-National Research Council (NASH) on the marketing, clinical efficacy, and comment on each drug are set forth below.

The following OTC drugs are included in this announcement:

1. Isophorin Nose Drop Solution containing phenylephrine hydrochloride; Broemmelsiek Pharmaceuticals, 1235 Sutter Street, San Francisco, Calif. 94109 (NDA 16-444).

2. Propadrine Hydrochloride Elixir containing phenylpropanolamine hydrochloride; Merrick Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486 (NDA 1-205).


4. Tagatagh Tablets containing chlo-ropheniramine maleate, Lederle Laboratories, Division of American Cyanamid Co., Pearl River, N.Y. 10968 (NDA 8-331).

5. Histadryl and A.S.A. Compound Pulvules containing metapyrapone hydrochloride, phenacetin, mephenesin, and caffeine; Eli Lilly and Co. (NDA 6-340).


7. Decapryl with Aspirin, Phenacetin, and Caffeine Tablets containing doxylamine succinate, aspirin, phenacetin, and caffeine; Merrell-National Laboratories, Division of Richardson-Merrell Inc., 110 East Amity Road, Cincinnati, Ohio 45215 (NDA 6-412).

8. Forthan Inhaler containing meth-yxycine; Eli Lilly & Co. (NDA 6-444).

9. Antistine-Privine Nasal Solution containing antazoline hydrochloride and naphazoline hydrochloride; Ciba Pharmaceutical Co. (NDA 6-486).

10. Wyamine-D Tablets containing mephentermine and menthol; Wyeth Laboratories, Division of Richardson-Merrell Inc., 122 East 42d Street, New York, N.Y. 10017 (NDA 6-562).

11. Wyamine Sulfate Nasal Solution containing mephentermine sulfate; Wyeth Laboratories (NDA 6-652).

12. Clopane Hydrochloride Solution containing cyclopentamine hydrochloride; Eli Lilly & Co. (NDA 6-666).

13. Corecidin Cold Tablets containing chlorpheniramine maleate, aspirin, phenacetin, and caffeine; Roche Laboratories, Inc., 340 Kingsland Avenue, Nutley, N.J. 07110 (NDA 6-696).


15. Thephorin-AC Tablets containing pheniramine maleate, aspirin, phenace-tin and caffeine; Roche Laboratories, Division of Hoffmann-La Roche Inc., 340 Kingsland Avenue, Nutley, N.J. 07110 (NDA 8-268).

16. Fedrazil Tablets containing chlorcyclizine hydrochloride and pseudoephedrine hydrochloride; Burroughs Wellcome Co. (NDA 11-876).


21. Tri-Span 12-Hour Decongestant Tablets containing acetaminophen, phenylpropanolamine hydrochloride, aspirin, phenylpropanolamine hydrochloride; Vick Chemical Co., Division of Richardson-Merrell Inc., 122 East 42d Street, New York, N.Y. 10017 (NDA 12-849).


The National Academy of Sciences-National Research Council, Drug Efficacy Study Group, Panel on Drugs for Relief of Pain, made the following General Statements on Analgesic Preparations, which are applicable to any of these products that make analogous claims.

**General Statements on Analgesic Preparations**

**Evidence for General Analgesic Effect**

It is the recommendation of the Panel that, when a drug has been shown to be an effective analgesic in several different kinds of clinical pain, by suitably controlled trials using modern criteria, such a drug be entitled to consideration as an "all-purpose" analgesic. Unidentified pain, indicating that this is not appropriate. In such cases, it would seem desirable to allow the use of the product for the relief of most kinds of pain, thus avoiding the necessity for listing specific conditions.

**Analgesic Mixtures**

There is increasing evidence, which has accumulated particularly within the past few years, that it is not unusual for there to be an effect of adding one drug to another. Thus, drugs may merely summate in their activities, synergize each other, or produce true potentiating. Since adequate trials on the relative efficacy of single drugs and mixtures are usually unavailable, the Panel to be both fair and scientific in the evaluation of many of the mixtures which have been asked to be reviewed.

Furthermore, some ingredients appear to have been added to these mixtures on the basis of rationale that is not supported by the Panel. On other occasions, the rationale

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seems evident, but the reason for the particular drug prescribed (especially those which seem homeopathic) is not clear.

In addition to the well-known objections that many analgesics do not allow flexibility in the doses of individual ingredients, one can object to many analgesic mixtures because they contribute little additional therapeutic benefit, and are increasing the risk of side effects, allergic sensitization, etc. One can perhaps justify the use of some of these mixtures, at least at present, with some other symptom, such as a stuffy nose, and both symptoms can be handled reasonably well. However, we would promote such a mixture as an all-purpose remedy for all kinds of pain, including those which cannot possibly be aided by one or more of the ingredients, is, in the view of the Panel, to encourage bad therapeutics.

**SEMANTIC CONFUSION**

The words “synergism” and “potentiation” are subject to multiple interpretations, even among professional pharmacologists. It would seem desirable to avoid their use, focusing instead on a description of what actually occurs in the clinic and laboratory. The word “potency” also has different meanings to different persons. If one is talking simply about milligram potency, this is actually a measure of the clinical setting and, therefore, the term “potency” should probably be avoided.

**RELEVANT INFORMATION**

Many package inserts contain material of no relevance to most practitioners. For example, the animal data are often not helpful, and are not always clearly identifiable as such. Testing for one symptom seems to be accepted as a substitute for clinical data. Also irrelevant and not particularly helpful to the reader is a list of clinical testing data, only some of which bear on the points at issue, and most of which are uninterpretable because of defects in clinical design.

**DRUG DEPENDENCE AND ABUSE**

The following statement is proposed to bring uniformity to the claims made concerning the dependence-producing properties of narcotic analgesics and preparations containing narcotic analgesics. It is recognized that many of the claims concerning a lesser dependence-producing liability of specific narcotic analgesics reflect the fact that the particular drug claims a lesser common liability. However, it must also be recognized that the actual abuse rates do not accurately reflect dependence potential. It is known that agents and preparations that have not been commonly abused in some social settings at some times, have been extensively abused in other settings at other times.

One of the major purposes of the existing laws and regulations concerning narcotic analgesics is to prevent abuse. Therefore, all agents that have been shown to produce morphine-like physiologic and subjective changes should be administered in such a manner that will produce morphine-like dependence, or that will substitute for morphine in morphine-dependent individuals, shall carry the following recommended warning:

**WARNING**

(Name of agent) can produce dependence of the morphine type and therefore has the potential for being abused. The only exceptions to this recommendation are substances specifically exempted from this warning by the Federal law or regulation.

**RIGID Dose RECOMMENDATIONS**

The Panel believes that doctors should not be bound by rigid recommendations given in package inserts. These recommendations represent advice as to the doses at which most patients can be treated and the need for which the needs of most patients can be met. However, it is good practice to manipulate the doses until a therapeutic failure, or in the event of untoward effects. Furthermore, tolerance to a drug may develop, and may require an increase in dose. It is the Panel's observation that some of the recommended doses are too low.

**DEFICIENCIES OF METHODOLOGY**

There is a need for additional methodology for the study of pain. Thus, for example, there is no way of assessing on the comparative effects of analgesics given repeatedly to patients with chronic pain. The result with single doses may or may not be transferable to such situations. Another area of deficiency is the evaluation of topical ointments that produce obvious sensations of cooling or warmth. Such limitations in methodology should be kept in mind by the Food and Drug Administration when evaluating data on drugs, both old and new.

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

1. Loperamide Hydrochloride Spray containing phenylephrine hydrochloride. This drug has been evaluated by the Panel on Drugs Used in Allergy.
   - Indication: Symptomatic relief (of nasal congestion) in colds, sinusitis, and hay fever.
   - Evaluation: Effective.
   - Comments: None.

2. Propadine Hydrochloride Elixir containing phenylpropanolamine hydrochloride. This drug has been evaluated by the Panel on Drugs Used in Allergy.
   - Indication: Hay fever and allergic rhinitis.
   - Evaluation: Probably effective.
   - Comments: The Panel believes that this product is effective, adequately controlled clinical studies have not been presented.

3. Pravilin Hydrochloride Nasal Jelly, Nasal Solution, and Nasal Spray containing naphazoline hydrochloride. This drug has been evaluated by the Panel on Drugs Used in Allergy.
   - Indication: Relief of nasal congestion, as in colds, sinusitis, and hay fever.
   - Evaluation: Probably effective.
   - Comments: The data presented by the Panel on Drugs Used in Allergy, this is an effective product, but adequate documentation has not been provided.

4. Tussionex Inhaler containing tanamine, noicephrine, and menthol. This drug has been evaluated by the Panel on Drugs Used in Allergy.
   - Indication: Relief of nasal congestion.
   - Evaluation: Possibly effective.
   - Comments: Data relevant to this mode of administration of this compound have not been presented to the Panel.

5. Tagalyn Tablets containing chlorothiazide. This drug has been evaluated by the Panel on Drugs Used in Allergy.
   - Indication: Temporary relief of nasal congestion, watering of the eyes, running nose and sneezing due to hay fever or rain fever.
   - Evaluation: Possibly effective.
   - Comments: Adequate documentation of the clinical effect of this compound at the recommended dose has not been presented to the Panel.

6. Histadrin and A.S.A. Compound Pulvules containing methadylene hydroxybenzoil benzoate, aspirin, phenylpropanolamine, and caffeine. This drug has been evaluated by the Panel on Drugs Used in Allergy.
   - Indication: Relief of symptoms of the common cold.
   - Evaluation: Effective, but * * *(subsequently reevaluated as ineffective as a fixed combination).
   - Comments: It has not been proved that the antihistamine contributes to the relief of these symptoms provided by 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. However, it has not been proved for a cold, antihistamines may be effective, but antihistamines is being treated in that instance, not an upper respiratory infection.
   - General comments: A warning about the dangers of use by aspirin-sensitive patients should be included on the label.

7. Benzedrex Inhaler containing propylxynadrine and menthol. This drug has been evaluated by the Panel on Drugs Used in Allergy.
   - Indication: Temporary relief of nasal congestion in colds and hay fever; also for ear block and pressure pain during air travel.
   - Evaluation: Possibly effective.
   - Comments: Although the Panel believes that this product is effective, adequately controlled studies supporting its efficacy have not been presented.

8. Decapryn with aspirin, phenacetin and caffeine tablets containing doxylamine succinate, aspirin, phenacetin, and caffeine. This drug has been evaluated by the following Panels:
   - a. Panel on Drugs Used in Allergy.
   - b. Panel on Drugs for Relief of Pain.
   - c. Panel on Drugs Used in Allergy.
   - d. Panel on Drugs Used in Allergy.
   - Indication: Temporary relief of minor discomforts associated with the common cold.
   - Evaluation: Effective, but * * * (subsequently reevaluated as ineffective as a fixed combination).
   - Comments: It has not been proved that the antihistamine contributes to the relief of these symptoms provided by 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 mistakenly mistaken for a cold, antihistamines may be of benefit, but allergic rhinitis is being treated in that instance, not an upper respiratory infection.
   - General comments: A warning about the dangers of use by aspirin-sensitive patients should be included on the label.

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


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

Indication: Relief of nasal congestion.

Evaluation: Probably effective.

Comments: In the experience of the Panel, this is an effective product, but adequate documentation has not been provided.

10. Antistine-Privine Nasal Solution containing antazoline hydrochloride and naphazoline hydrochloride.

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

Indication: Symptomatic relief of nasal congestion due to allergic rhinitis; vasomotor rhinitis; acute, subacute or chronic sinusitis.

Evaluation: Probably effective.

Comments: In the experience of the Panel, this is an effective product, but adequate documentation has not been provided.

11. Wyamine Inhaler containing mephentermine and menthol.

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

Indication: Temporary relief of nasal congestion.

Evaluation: Possibly effective.

Comments: The Panel is unaware of any acceptable evidence to support this.

General comments: The label should warn that prolonged or excessive use of this product may result in rebound nasal congestion.


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

Indication: Nasal decongestion in acute or chronic rhinitis, sinusitis, and allergic rhinitis (hay fever and perennial or vasomotor rhinitis).

Evaluation: Probably effective.

Comments: In the experience of the Panel, this is an effective product. However, adequately controlled studies do not seem to be available.

13. Clopane Hydrochloride Solution containing cyclopentamine hydrochloride.

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

Indication: Nasal congestion due to hay fever, chronic rhinitis, or the common cold, sinusitis; preoperative vascularization of nasal and nasopharyngeal mucosa; and prophylaxis to nasal congestion.

Evaluation: Probably effective.

Comments: This judgment is based on physiologic studies, in the absence of adequate clinical studies.

14. Coricidin Cold Tablets containing chlorpheniramine maleate, aspirin, and caffeine.

This drug has been evaluated by the following Panels:

a. Panel on Drugs Used in Allergy.

b. Panel on Drugs for Relief of Pain.

Evaluation: Effectively, but ** (subsequently reevaluated as ineffective as a fixed combination).

Comments: It has not been proved that the antihistamine contributes to the relief of these symptoms provided by 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, an antihistamine may be of benefit; but allergic rhinitis is being treated in that instance, not an upper respiratory infection.

General comments: The presence of aspirin in this combination should be clearly identified and a warning about the dangers of use by aspirin-sensitive patients should be included on the label.

15. Theophorin-AC Tablets containing phenindamine tartrate, aspirin, phenacetin, and caffeine.

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

Indication: Relief of "cold symptoms."

Evaluation: Effective, but ** (subsequently reevaluated as ineffective as a fixed combination).

Comments: It has not been proved that the antihistamine contributes to the relief of these symptoms provided by 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.

General comments: A warning about the dangers of use by aspirin-sensitive patients should be included on the label.

16. Vasoxyl nasal solution and spray containing methoxamine hydrochloride.

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

Indication: Temporary relief of nasal congestion.

Evaluation: Probably effective.

Comments: In the experience of the Panel, this is an effective product. However, adequately controlled studies do not seem to be available.

General comments: The labeling should warn that excessive or prolonged use of this product may result in rebound nasal congestion.

17. Beno-fedrin solution containing diphenhydramine hydrochloride, and ephedrine hydrochloride.

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

Indication: Relief of congestion of the mucous membrane of the nose and throat.

Evaluation: Effective, but **.

Comments: No data have been presented to the Panel that demonstrate the superiority of this combination to ephedrine alone. No data demonstrating the local effect of the antihistamine have been presented to the Panel, other than some data regarding local anesthetic properties. The usefulness of Chlorhexidine (chlorobutanol) has not been demonstrated.

The potential risk of sensitization to topically applied antihistamines is such that the Panel prefers the oral route. As indicated above, antihistaminic efficacy is not well established for most of these drugs when they are applied directly to the nasal mucosa.

This indication was reevaluated as possible, with this product.

No data has been presented to the Panel demonstrating benefit in adding antihistamine to Chlorhexidine to the mixture.

General comments: The potential risk of sensitization to topically applied antihistamines is such that the Panel feels this is another reason not to use the product.

Finally, the label should warn that prolonged or excessive use of this product may result in rebound nasal congestion.

General comments: The label should warn that prolonged or excessive use of this product may result in rebound nasal congestion.

18. Inhison-APC Tablets containing pheniramine maleate, aspirin, phenacetin, and caffeine.

This drug has been evaluated by the following Panels:

a. Panel on Drugs Used in Allergy.

b. Panel on Drugs for Relief of Pain.

Evaluation: Effectively, but ** (subsequently reevaluated as ineffective as a fixed combination).

Comments: It has not been proved that the antihistamine contributes to the relief of these symptoms provided by 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.

Evaluation: Effectively, but **.

Comments: The APC component probably does not add to the effect of the antihistamine. Pheniramine probably is an effective antihistamine when taken in adequate dosage. The amount of antihistamine present in this product is below that found to be effective in the experience of the Panel.

General comments: A warning about the dangers of use by aspirin-sensitive patients should be included on the label.
Evaluation: Effective, but ** *.

Comments: This combination contains the known analgesic combination, APC, which at the recommended dose would provide relief of pain. There is no reason to expect that the additional ingredient 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, and conclusive studies on the above-mentioned conditions.

General comments: Whether the addition of the additional ingredient contributes anything additional to the management of the clinical entities of “aches, pains, and simple headache” is not known.

20. Phenylpropanolamine Hydrochloride and Phenylpropanolamine Timed Release Capsule: This drug has been evaluated by the Panel on Drugs Used in Allergy.

Indication: Relief of nasal congestion due to the common cold.

Evaluation: Possibly effective.

Comments: No data supporting this claim have been presented to the Panel.

21. Fedral Tablets containing chlorcyclizine hydrochloride and pseudophedrine hydrochloride.

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

Indication: Relief of nasal congestion associated with colds.

Evaluation: Possibly effective (subsequently reevaluated as ineffective as a fixed combination).

Comments: There is no evidence that either drug in this combination will accomplish what is claimed. The dose of pseudophedrine is less than optimal for many adults and it has not been proved to be beneficial for this indication. It has not been proved that the antihistamine contributes to the relief of cold symptoms which is provided by 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.

General comments: A warning about the dangers of use of aspirin-sensitive patients should be included on the label.

Panel on Drugs Used in Dentistry

Indication: To aid in the relief of pain and discomfort following tooth extraction or other dental work.

Evaluation: Possibly effective.

Comments: There is no question that APC is effective in controlling pain of dental origin. However, the claim that the combination of phenyltoloxamine in the listed claims, and further questions its low dosage. The Panel feels that the dose should substantiate the use of phenyltoloxamine in this dose as effective in the treatment of the listed conditions.

Panel on Drugs for Relief of Pain

Indication: Pain-relieving compound with antihistamine.

Evaluation: Effective, but ** *

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

Indication: For relief of discomfort from colds, headaches, minor menstrual and dental pain.

Relieves muscular aches and pains, feverish feeling, headache.

Evaluation: Effective, but ** *.

Comments: This combination contains the known analgesic, APC, which at the recommended dose would provide relief of pain. There is no reason to expect that the additional ingredient, Branidril, 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, and conclusive studies on the above-mentioned conditions.

General comments: Whether the additional ingredient contributes anything additional to the management of the clinical entities of “aches, pains, and simple headache” is not known.


This drug has been evaluated by the following Panels:

a. Panel on Drugs Used in Allergy.

Evaluation: Effective, but ** *.

Comments: Adequate documentation of these claims has not been supplied. Phenyltoloxamine is a weak antihistamine, in the experience of the Panel, and there is no controlled study supporting its usefulness in colds. Aspirin is not an effective nasal decongestion known to the Panel, although it is a known analgesic.

b. Panel on Drugs for Relief of Pain

Indication: New Quadrin’s acid-free formula works without aspirin to shut out pain. Quadrin’s new analgesic and antihistamine is safer, faster than aspirin.

Evaluation: Effective, but ** *.

Comments: No supporting data, collected in a controlled fashion, have been presented to the Panel. It is doubtful that the antihistamine is of benefit for the relief of nasal congestion due to the common cold. Several 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:

It has not been proved that the antihistamine contributes to the relief of cold symptoms which is provided by 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.

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[DESI 7909]

CERTAIN PARENTERAL DRUGS CONTAINING VERATRUM ALKALOIDS

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 drugs:

1. Veratrum Injection containing protovatrin A and B; the Dow Chemical Co., 1200 Madison Avenue, Indianapolis, Ind. 46222 (NDA 8-708).

2. Uniken Fm Aqueous containing cypexetamine acetate; Mallinckrodt Chemical Works, 3600 North Second Street, St. Louis, Mo. 63160 (NDA 8-814).

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 new-drug applications provided that such drug is regulated as a new drug. 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 reports, as well as other available evidence, and concludes that these drugs are effective for short-term use in the treatment of hypertensive crises.

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 veratrum alkaloid preparations are aqueous solutions suitable for parenteral administration.

2. Labeling conditions.

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

b. The drugs are labeled to comply with all requirements of the Act and regulations. Their labeling bears adequate information for safe and effective use and, where applicable, the Academy's comments. The "Indications" sections are as follows:

INDICATIONS

For short-term use in the treatment of hypertensive crises.


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 "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 and an abbreviated supplement for updating information is as described in paragraphs (a)(1)(i) and (iii) of the notice of July 14, 1970.

b. For any person who does not hold an approved or effective new-drug ap-