



**EXHIBIT 1**

and ulcerative lesions resulting from trauma.

A supplemental new-drug application is invited to revise the labeling provided for in the new-drug application for the above preparation to limit the claims and present the conditions of use as follows:

#### ACTIONS

Triamcinolone acetonide is a synthetic corticosteroid and possesses properties of an anti-inflammatory, antipruritic, and anti-allergic nature. The emollient dental paste acts as an adhesive vehicle for applying the active medication to oral tissues. The protective action of the adhesive vehicle may serve to reduce the pain associated with oral irritation.

#### INDICATIONS

Indicated for adjunctive treatment and for the temporary relief of symptoms associated with oral inflammatory lesions and ulcerative lesions resulting from trauma.

#### CONTRAINDICATIONS

Fungal, viral, or bacterial infections of the oral mucosa. Hypersensitivity to any component.

#### WARNING

**USE IN PREGNANCY:** Safe use in pregnancy has not been established.

#### PRECAUTIONS

Patients with tuberculosis, peptic ulcer, or diabetes mellitus should not be routinely treated with this steroid preparation.

It should be borne in mind that the normal defensive responses of the oral tissues are depressed in patients receiving topical corticosteroid therapy. Virulent strains of oral microorganisms may multiply without producing the usual warning symptoms of oral infections.

If significant regeneration or repair of oral tissues has not occurred in 7 days, additional investigation into the etiology of the oral lesion is advised.

#### ADVERSE REACTIONS

Prolonged administration may elicit the adverse reactions known to occur with systemic steroid preparations; for example, adrenal suppression, alteration of glucose metabolism, protein catabolism, peptic ulcer activations, and others. These are usually reversible and disappear when the hormone is discontinued.

#### DOSAGE AND ADMINISTRATION

The drug should be applied 2 to 3 times a day following meals and at bedtime. If significant repair or regeneration has not occurred in 7 days, further investigation is advisable.

The holder of the new-drug application for the drug listed above has been mailed a copy of the NAS-NRC report together with a copy of the labeling conditions in this announcement. Any manufacturer, packer, or distributor of a drug of similar composition and labeling to the drug listed in this announcement or any other interested person may obtain a copy of the NAS-NRC report by writing to the Food and Drug Administration, Press Relations Office, 200 C Street SW., Washington, D.C. 20204.

Written comments regarding this announcement may be addressed to the Special Assistant for Drug Efficacy Study Implementation, Bureau of Medicine, Food and Drug Administration, 200 C

Street SW., Washington, D.C. 20204.

This statement 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: June 18, 1968.

J. K. Kirk,  
Associate Commissioner  
for Compliance.

[F.R. Doc. 68-7587; Filed, June 25, 1968;  
8:50 a.m.]

### DRUGS FOR HUMAN USE

#### Drug Efficacy Study Implementation Announcement Regarding Salt Substitutes

The Food and Drug Administration has received reports from the National Academy of Sciences—National Research Council, Drug Efficacy Study Group, on the following salt substitute preparations:

1. Dialal, marketed by E. Fougere and Co., Inc., East Cantigue Road, Hicksville, Long Island, N.Y. 11802.
2. Neocurtasal, marketed by Winthrop Laboratories, 90 Park Avenue, New York, N.Y. 10016.
3. Co-Salt, marketed by U.S. Vitamin and Pharmaceutical Corp., 800 Second Avenue, New York, N.Y. 10017.

Such preparations are regarded by the Food and Drug Administration as foods and are subject to the food provisions of the Federal Food, Drug, and Cosmetic Act, including section 403(j) concerning foods for special dietary uses (21 U.S.C. 343(j)). They should be suitably labeled to comply with Part 125 (21 CFR Part 125), the current regulations for foods for special dietary uses, including § 125.9 *Label statements relating to certain foods used as a means of regulating the intake of sodium in dietary management.*

These preparations are also regarded as drugs and are thus subject to the drug provisions of the act. They should bear a cautionary statement to the effect that they should not be used without the advice of a physician.

Attention is directed to the public hearing on foods for special dietary uses that was scheduled to begin June 20, 1968, in Room 5131, Health, Education, and Welfare Building North, 330 Independence Avenue SW., Washington, D.C., involving issues that will relate to this announcement. Notice of the hearing was published in the FEDERAL REGISTER of April 2, 1968; 33 F.R. 5268.

At a later date it will be proposed that the subject preparations be added to paragraph (b) of § 130.302 *List of drugs for human use that do not now require an approved new-drug application* (21 CFR 130.302), Section 130.302 was included in a notice of proposed rule-making published in the FEDERAL REGISTER of May 28, 1968 (33 F.R. 7762).

The holders of new-drug applications for the drugs listed above have been mailed a copy of the NAS-NRC report.

Any other manufacturer, packer, or distributor of such drugs or any other interested person may obtain a copy of the NAS-NRC report by writing to the Food and Drug Administration, Press Relations Office, 200 C Street SW., Washington, D.C. 20204.

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: June 18, 1968.

J. K. Kirk,  
Associate Commissioner  
for Compliance.

[F.R. Doc. 68-7588; Filed, June 25, 1968;  
8:50 a.m.]

### DRUGS FOR HUMAN USE

#### Drug Efficacy Study Implementation Announcement Regarding Certain Iron Preparations for Parenteral Use

The Food and Drug Administration has reviewed and evaluated reports from the National Academy of Sciences—National Research Council, Drug Efficacy Study Group, on the following iron preparations for parenteral use:

1. Astrafer injection; 100 milligrams of trivalent iron (as dextriferron) per 5 milliliters; marketed by Astra Pharmaceutical Products, Inc., 7 Neponset Street, Worcester, Mass. 01606.
2. Imferon injection; 50 milligrams of trivalent iron (as iron dextran) per milliliter; marketed by Lakeside Laboratories, Inc., 1707 East North Avenue, Milwaukee, Wis. 53201.

The Food and Drug Administration concurs in the conclusions of the Academy that these drugs are shown to be effective and suitable for the treatment of iron-deficiency anemia when established conditions exist corroborating iron deficiency anemia not amenable to oral therapy.

The active components of preparations of this kind are complexes of iron and modified carbohydrates. Because of the potential for toxicity associated with the use of these drugs and the fact that their integrity is dependent to a large degree upon manufacturing procedures, such preparations continue to be regarded as new drugs (21 U.S.C. 321(p)).

The holders of previously approved new-drug applications for these articles are herewith exempted, pursuant to § 130.35(d), from the annual reporting requirements of §§ 130.35(e) and 130.13(b)(4) of the new-drug regulations (21 CFR 130.13(b)(4), 130.35(e), (f)).

The holders of such new-drug applications are invited to submit new-drug application supplements to provide for revising the labeling so that the parts of the labeling indicated are substantially as described below and include the box warning at the beginning of any labeling piece:

**WARNING:** The parenteral use of complexes of iron and carbohydrates has resulted in fatal anaphylactic-type reactions. Deaths associated with such administration have been reported. Therefore, -----\* should be used only in those patients where clearly established indications exist, confirmed by appropriate laboratory investigations corroborating iron deficiency anemia not amenable to oral iron therapy.

\*Name of drug.

#### ACTIONS

Ferric iron administered parenterally is transported by transferrin and incorporated into hemoglobin.

#### INDICATIONS

For the treatment of iron deficiency anemia: Intramuscular or intravenous injections of iron are advisable solely for use in those patients in whom iron deficiency anemia is present, its cause has been determined and, if possible, corrected, and in whom oral administration of iron is unsatisfactory or impossible; for example:

Intolerance to oral preparations;  
Resistance to oral iron therapy;  
Rapid replenishment of iron stores in selected patients in whom oral therapy is ineffective, such as hypochromic anemia of infancy and hypochromic anemia of the last trimester of pregnancy;  
Selected hemorrhagic cases (appropriate steps should be taken to correct and prevent any excessive blood loss that may have been revealed as an etiologic factor);

To replace postoperative transfusion to some degree;

In those patients who cannot be relied upon to take oral medication.

#### CONTRAINDICATIONS

Hypersensitivity to the product.  
All anemias other than iron deficiency anemia.

#### WARNINGS

This preparation should be used with extreme care in the presence of serious impairment of liver function.

A risk of carcinogenesis may attend the injection of iron-carbohydrate complexes. Such complexes have been found under experimental conditions to produce sarcomas when injected in rats, mice, and rabbits, and possibly in hamsters, in very large doses. The number of tumors produced was relatively small, and such tumors have not been produced in guinea pigs. The risk of carcinogenesis in man following recommended therapy appears to be extremely small; however, the long latent period between the injection of a potential carcinogen and the appearance of a tumor makes it impossible as yet to measure the risk in man.

#### PRECAUTIONS

Improper therapy with these agents will cause storage of iron with the consequent possibility of exogenous hemosiderosis. Such iron overload is particularly apt to occur with patients with hemoglobinopathies and other refractory anemias which might be erroneously diagnosed as iron deficiency anemia.

#### ADVERSE REACTIONS

Intramuscular injection: Variable degree of soreness and inflammation; brownish discoloration in the area of injection.

Intramuscular and intravenous injections: Anaphylactoid and anaphylactic reactions, including fatal anaphylactic reactions; severe febrile reactions.

#### DOSEAGE AND ADMINISTRATION

Periodic hematologic determinations are to be used as a guide in therapy, bearing in mind that iron storage may lag behind the

appearance of normal blood morphology. The total cumulative amount required to restore hemoglobin and replenish iron stores may be approximated from the formula:

$$0.3 \times \text{Body weight in pounds} \times (100 - \frac{\text{Patient's hemoglobin in gram percent} \times 100}{14.8}) = \text{Milligrams total iron to be injected}$$

#### DOSEAGE FOR INTRAMUSCULAR PREPARATIONS

Each day's dose should ordinarily not exceed 25 milligrams for infants under 10 pounds, 50 milligrams for children under 20 pounds, 100 milligrams for patients under 110 pounds, and 250 milligrams for others.

#### DOSEAGE FOR INTRAVENOUS PREPARATIONS

To minimize toxic reactions, the initial dose should be limited to 15 to 30 milligrams followed by daily increments for 2 or 3 days until a 100-milligram daily dose is reached. This larger dose should be given slowly (1 minute per 20 to 50 milligrams).

The holders of the new-drug applications for the drugs listed above have been mailed a copy of the NAS-NRC report along with a copy of the labeling conditions contained in this announcement. Any manufacturer, packer, or distributor of a drug of similar composition and labeling to the drugs listed in this announcement, or any other interested person, may obtain a copy of the NAS-NRC report by writing to the Food and Drug Administration, Press Relations Office, 200 C Street SW., Washington, D.C. 20204.

Written comments regarding this announcement may be addressed to the Special Assistant for Drug Efficacy Study Implementation, Bureau of Medicine, Food and Drug Administration, 200 C Street SW., Washington, D.C. 20204.

This notice is issued pursuant to the provisions of the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502 (a), (f), 505, 52 Stat. 1041, 1050-53, as amended; 21 U.S.C. 321(p), 352 (a), (f), 355) and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: June 18, 1968.

JAMES L. GODDARD,

Commissioner of Food and Drugs.

[F.R. Doc. 68-7589; Filed, June 25, 1968; 8:50 a.m.]

## CIVIL AERONAUTICS BOARD

[Agreement CAB 5044-A136; Order E-26946]

### AIR TRAFFIC CONFERENCE OF AMERICA

#### Order Deferring Action Regarding Advertised Tours

Adopted by the Civil Aeronautics Board at its office in Washington, D.C., on the 20th day of June 1968.

On March 19, 1968, the Air Traffic Conference of America (ATC) filed pursuant to section 412 of the Federal Aviation Act of 1958, as amended, the following amendment to the Agency Resolution adopted at the Agency Committee meet-

ing of January 16-18, 1968, for intended effectiveness June 1, 1968:<sup>1</sup>

Resolved, that effective June 1, 1968, section XII.B.1, Resolution 80.10, be amended to read as follows:

"Advertised Air Tour" means a complete package, as set forth in Paragraph C of this section, advertised in a Tour Folder, offered for sale to the public, and prepaid in full by the purchaser: *Provided*, That in connection with travel to or from conventions or meetings, lodgings and other ground arrangements directly connected with the convention or meeting program shall not be considered a part of the "complete package."

An advertised air tour, to qualify for the 10 percent commission must include, in addition to lodging for a minimum of two nights, at least two meals per day and at least one additional feature such as a sightseeing trip, etc., in addition to the air transportation involved.<sup>2</sup> Thus, the effect of the amendment is to make it more difficult for a tour connected with a convention or meeting to qualify as an advertised air tour and thereby entitle the agent to a 10 percent rather than a 5 or 7 percent commission.

The American Society of Travel Agents (ASTA), Don Travel Service, Inc., New York, and Belts Travel Service, Inc., San Francisco, oppose the amendment. ATC submitted a letter of clarification and explanation.

It appears from ATC's letter that the resolution is based on the assumption that persons attending meetings and conventions do so for reasons other than the promotional efforts of the agents. As a consequence, the agents are not entitled to a 10 percent commission but rather the normal commission rates should apply. ATC also attempted to give meaning and content to the words convention and meetings.

ASTA and the individual agents contend that over the years agents have promoted and developed tours associated with conventions and meetings to the benefit of all concerned, including the airlines. According to the objectors, by reducing the commission and tightening the definition of an advertised air tour, the resolution will make it more difficult for the agents to promote domestic tour travel. It is argued that such a result is contrary to the efforts of all concerned to promote domestic travel.

On the basis of the record to date, the Board is unable to act upon the matter. Except for the submission of several brochures describing advertised air tours

<sup>1</sup> ATC has agreed on behalf of its members to withhold implementation of the amendment until the Board acts on the matter.

<sup>2</sup> An exception is provided which permits the Advertised Air Tour Committee of ATC to approve any package by two-thirds majority vote.