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NUMBER 4

Pediatrics

AMERICAN ACADEMY OF PEDIATRICS ELK GROVE VILLAGE IL 60009–0927

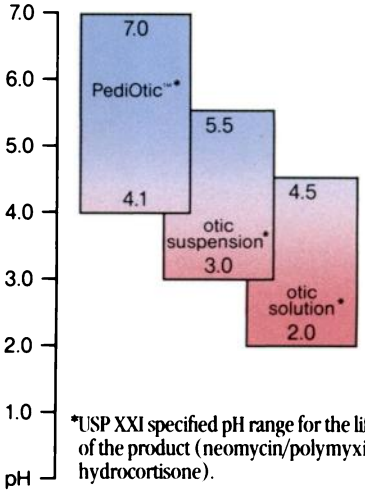
PEDIAU 82(4) pp. 527–681 (1988)

NEW

PediOtic™ suspension sterile

Formulated to be less acidic to help minimize irritation.

A more normal pH range means less potential for painful irritation.



*USP XXI specified pH range for the life of the product (neomycin/polymyxin B/ hydrocortisone).

Formulated to help take the sting out of otitis externa therapy

New PediOtic™ suspension is specially formulated to have a higher pH range than conventional otics.

Children may be less likely to resist its instillation, and their parents will appreciate the ease of compliance.

And you can prescribe new PediOtic suspension with confidence, knowing it contains the same proven antibiotic/anti-inflammatory combination physicians have trusted for years.

Now there's a gentle effective treatment for "swimmer's ear" to please patient, parent, *and* physician.

PediOtic™ suspension sterile

Wellcome

(polymyxin B sulfate-neomycin sulfate-hydrocortisone)

brief summary

NEW PediOtic™ suspension sterile

(polymyxin B sulfate-neomycin sulfate-hydrocortisone)

DESCRIPTION: Pediotic suspension (polymyxin B sulfate-neomycin sulfate-hydrocortisone) is a sterile antibacterial and anti-inflammatory suspension for otic use. Each ml contains: Aerosporin® (polymyxin B sulfate) 10,000 units, neomycin sulfate equivalent to 3.5 mg neomycin base, and hydrocortisone 10 mg (1%). The vehicle contains thimerosal 0.001% (added as a preservative) and the inactive ingredients cetyl alcohol, glyceryl monostearate, mineral oil, polyoxyl 40 stearate, propylene glycol, and Water for Injection. Sulfuric acid may be added to adjust pH. Pediotic suspension has a minimum pH of 4.1, which is less acidic than the minimum pH of 3.0 for Cortisporin® Otic Suspension. **INDICATIONS AND USAGE:** For the treatment of superficial bacterial infections of the external auditory canal caused by organisms susceptible to the action of the antibiotics, and for the treatment of infections of mastoidectomy and fenestration cavities caused by organisms susceptible to the antibiotics. **CONTRAINDICATIONS:** This product is contraindicated in those individuals who have shown hypersensitivity to any of its components, and in herpes simplex, vaccinia, and varicella infections. **WARNINGS:** This product should be used with care in cases of perforated eardrum and in longstanding cases of chronic otitis media because of the possibility of ototoxicity. Neomycin sulfate may cause cutaneous sensitization. A precise incidence of hypersensitivity reactions (primarily skin rash) due to topical neomycin is not known. When using neomycin-containing products to control secondary infection in the chronic dermatoses, such as chronic otitis externa or stasis dermatitis, it should be borne in mind that the skin in these conditions is more liable than is normal skin to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low-grade reddening with swelling, dry scaling and itching, it may be manifest simply as a failure to heal. Periodic examination for such signs is advisable, and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for the patient thereafter. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If the infection is not improved after one week, cultures and susceptibility tests should be repeated to verify the identity of the organism and to determine whether therapy should be changed. Treatment should not be continued for longer than ten days. Allergic cross-reactions may occur which could prevent the use of any or all of the following antibiotics for the treatment of future infections: kanamycin, paromomycin, streptomycin, and possibly gentamicin. **ADVERSE REACTIONS:** Neomycin occasionally causes skin sensitization. Ototoxicity and nephrotoxicity have also been reported (see WARNINGS section). Adverse reactions have occurred with topical use of antibiotic combinations including neomycin and polymyxin B. Exact incidence figures are not available since no denominator of treated patients is available. The reaction occurring most often is allergic sensitization. In one clinical study, using a 20% neomycin patch, neomycin-induced allergic skin reactions occurred in two of 2,175 (0.09%) individuals in the general population.[1] In another study, the incidence was found to be approximately 1%.[2] The following local adverse reactions have been reported with topical corticosteroids, especially under occlusive dressings: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. Stinging and burning have been reported rarely when this drug gained access to the middle ear. **HOW SUPPLIED:** Bottle of 7.5 ml with sterilized dropper. NDC 0081-0910-02. Store at 15° to 25°C (59° to 77°F).

REFERENCES: 1. Leyden JJ, Kligman AM: Contact dermatitis to neomycin sulfate. *JAMA* 1979;242:1276-1278. 2. Prystowsky SD, Allen AM, Smith RW, et al: Allergic contact hypersensitivity to nickel, neomycin, ethylenediamine, and benzocaine. *Arch Dermatol* 1979;115:959-962.

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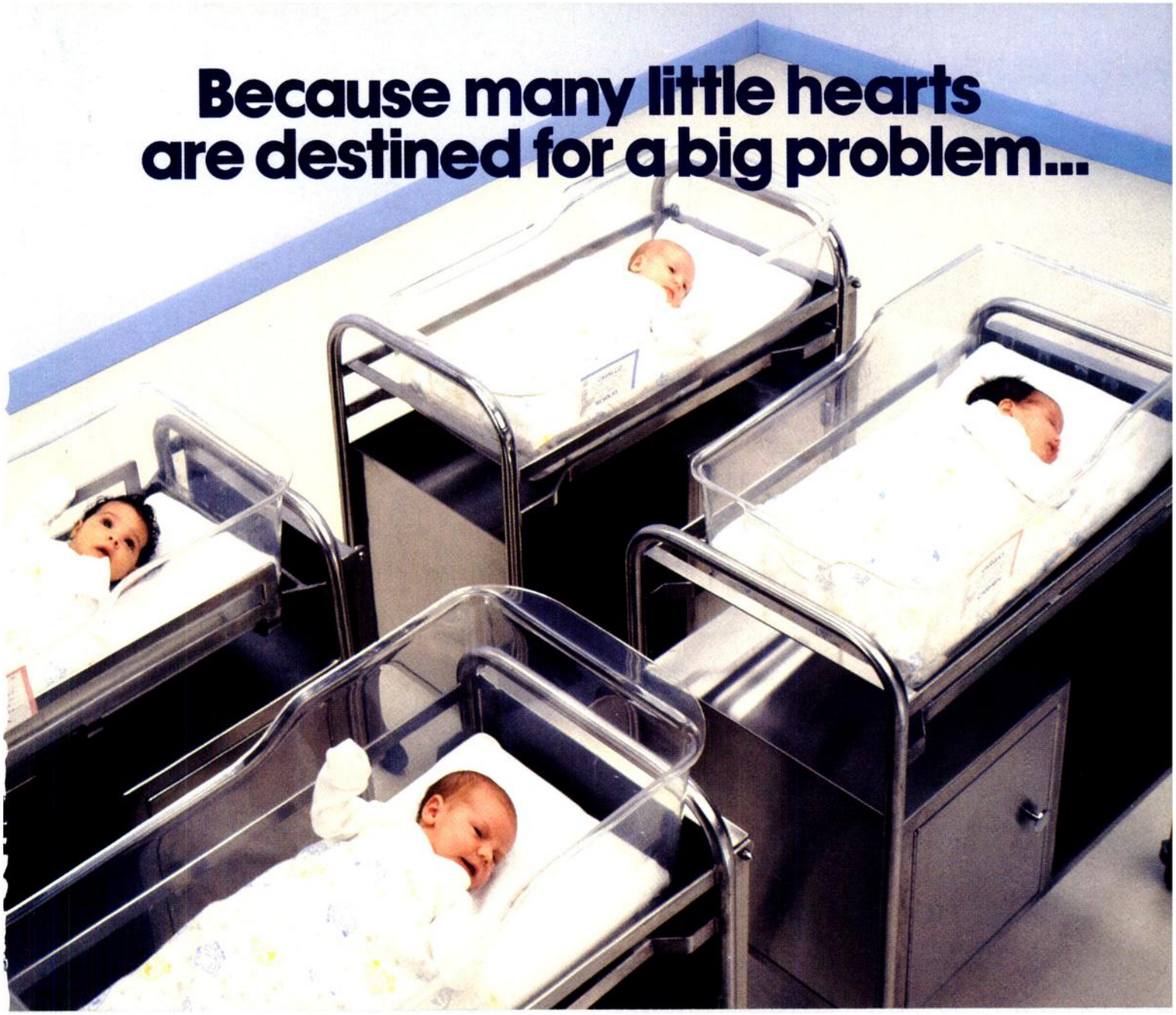
PED-100

Because many little hearts are destined for a big problem...



Fatty streaks in the aortas of 3-year-olds Fatty streaks have been found even in the aortas of 3-year-olds. Aortic fatty streaks have been strongly related to both total- and LDL-cholesterol levels and inversely to the HDL/LDL + VLDL ratio. Expert advice suggests that a rational approach to the prevention of CVD should begin early in life.[1]

SMA® maintains high levels of cardio-protective HDL Wyeth's SMA, with a lipid profile virtually identical to mother's milk, provides infants with HDL-cholesterol plasma levels that closely approximate those found in breast-fed infants. And, like breast milk, SMA has more than twice the level of monounsaturates than the other two leading formulas. High levels of monounsaturates have been associated with higher levels of cardio-protective HDL.[2] Start them early...and start them right... with SMA.

References: 1. Newman WP III, *et al:* Relation of serum lipoprotein levels and systolic blood pressure to early atherosclerosis. *N Engl J Med 314*:138-144, 1986. **2.** Mattson FH, Grundy SM: Comparison of effects of dietary saturated, monounsaturated and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. *J Lipid Res 26*:194-202, 1985.

S·M·A™
Infant Formula

A first step in good cardiovascular nutrition

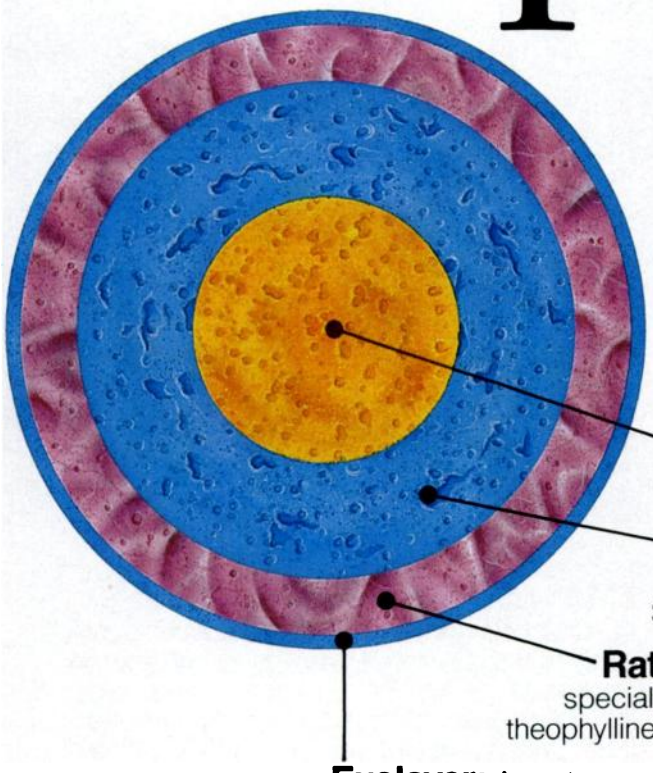
Important Notice. Breast milk is best for babies. Infant formula is intended to replace or supplement breast milk when breast-feeding is not possible or is insufficient, or when mothers elect not to breast-feed.
Good maternal nutrition is important for the preparation and maintenance of breast-feeding. Extensive or prolonged use of partial bottle-feeding, before breast-feeding has been well established, could make breast-feeding difficult to maintain. A decision not to breast-feed could be difficult to reverse.
Professional advice should be followed on the need for and proper method of use of infant formula and on all matters of infant feeding. Infant formula should always be prepared and used as directed. Unnecessary or improper use of infant formula could present a health hazard. Social and financial implications should be considered when selecting the method of infant feeding.

WYETH AYERST™

Slo-bid™
(theophylline, anhydrous)

THE SECRET OF CONSISTENT

It's complex



The complex design of Slo-bid™ is what makes it work consistently.

The micropellets within each Slo-bid capsule are designed with a built-in program of release, in order to ensure a constant rate of theophylline delivery throughout the dosing interval.

Inert nucleus: At the center is an inert nucleus that holds the entire system together.

Endomatrix: The nucleus is coated with a matrix of pure theophylline. Unlike Theo-Dur,* Slo-bid contains no free theophylline.[1]

Rate-controlling membrane: Hundreds of specialized pores regulate the slow, steady release of theophylline.

Exolayer: An outer-seal coat protects the system from abrasion and damage.

References:

1. Mansmann HC, Saccar CL: Experimental design to study sustained-release theophylline preparations. *J Asthma* 1984;21:359-363.
2. Hendeles L, Iafrate RP, Weinberger M: A clinical and pharmacokinetic basis for the selection and use of slow release theophylline products. *Clin Pharmacokinet* 1984;9:95-135.

*Theo-Dur is a registered trademark of Schering Corporation.

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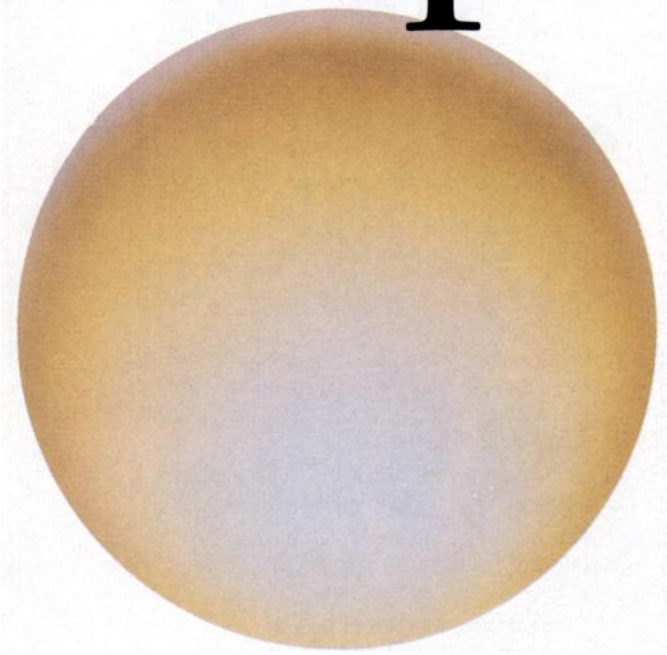

The simple result is greater dependability and less fluctuation in serum levels across dosage strengths than with Theo-Dur.[2]

In twelve hours, 100% of the theophylline in Slo-bid is released and at work, providing reliable serum levels. And, intact or sprinkled, Slo-bid has *one* release system for *all* dosage strengths, unlike Theo-Dur, which uses three different delivery systems.

Please see next page for brief summary of prescribing information.

In asthma, emphysema, bronchitis

Slo-bid™ 12

(theophylline, anhydrous)

The simple result of complex technology

Slo-bid™

50 mg, 100 mg, 200 mg, and 300 mg **Gyrocaps®**
Timed Release Capsules

INDICATIONS AND USAGE: For relief and/or prevention of symptoms from asthma and reversible bronchospasm associated with chronic bronchitis and emphysema.

CONTRAINDICATIONS: Slo-bid™ is contraindicated in individuals who have shown hypersensitivity to any of the components of this product.

WARNINGS: Status asthmaticus should be considered a medical emergency and is defined as that degree of bronchospasm which is not rapidly responsive to usual doses of conventional bronchodilators. Optimal therapy for such patients frequently requires both *additional medication*, parenterally administered and *close monitoring*, preferably in an intensive care setting.

Although increasing the dose of theophylline may bring about relief, such treatment may be associated with toxicity. The likelihood of such toxicity developing increases significantly when the serum theophylline concentration exceeds 20 μg/mL. Therefore, determination of serum theophylline levels is recommended to assure maximal benefit without excessive risk.

Serum levels above 20 μg/mL are rarely found after appropriate administration of the recommended doses. However, in individuals in whom theophylline plasma clearance is reduced *for any reason*, even conventional doses may result in increased serum levels of potential toxicity. Reduced theophylline clearance has been documented in the following readily identifiable groups: (1) patients with impaired renal or liver function, (2) patients over 55 years of age, particularly males and those with chronic lung disease, (3) those with cardiac failure from any cause, (4) neonates, and (5) those patients taking certain drugs (macrolide antibiotics and cimetidine). Decreased clearance of theophylline may be associated with either influenza immunization or active infection with influenza. Reduction of dosage and laboratory monitoring is especially appropriate in the above individuals.

Less serious signs of theophylline toxicity, i.e. nausea and restlessness, may appear in up to 50% of patients.

Unfortunately, however, serious side effects such as ventricular arrhythmias, convulsions, or even death may appear as the first sign of toxicity without any previous warning. Stated differently, *serious toxicity is not reliably preceded by less severe side effects.*

Many patients who require theophylline may exhibit tachycardia due to their underlying disease process so that the cause-effect relationship to elevated serum theophylline concentrations may not be appreciated.

Theophylline products may cause dysrhythmia and/or worsen preexisting arrhythmias and any significant change in rate and/or rhythm warrants monitoring and further investigation.

The occurrence of arrhythmias and sudden death (with histological evidence of necrosis of the myocardium) has been recorded in laboratory animals (minipigs, rodents, and dogs) when theophylline and beta agonists were administered concomitantly, although not when either was administered alone. The significance of these findings when applied to human usage is currently unknown.

PRECAUTIONS:

General: Mean half-life in smokers is shorter than non-smokers. Therefore, smokers may require larger or more frequent doses of theophylline. Morphine and curare should be used with caution in patients with airway obstruction as they may suppress respiration and stimulate histamine release. Alternative drugs should be used when possible.

Theophylline should not be administered concurrently with other xanthine preparations. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, alcoholism, liver disease, and in the elderly, especially males, and neonates. Great caution should be used in giving theophylline to patients with congestive heart failure. Frequently, such patients have shown markedly prolonged theophylline blood levels with theophylline persisting in serum for long periods following discontinuation of the drug. Use theophylline cautiously in patients with a history of peptic ulcer. Theophylline may occasionally act as a local gastrointestinal irritant, although GI symptoms are more commonly centrally mediated and associated with serum drug concentrations over 20 μg/mL.

Information for Patients: The physician should reinforce the importance of taking only the prescribed dose at the prescribed time intervals. The patient should alert the physician if symptoms occur repeatedly, especially near the end of a dosing interval. When prescribing administration by the sprinkle method, details of the proper technique should be explained to the patient.

Drug Interactions: Drug-Drug:

Toxic synergism with ephedrine has been documented and may occur with some other sympathomimetic bronchodilators. In addition, the following drug interactions have been demonstrated:

Drug	Effect
Aminophylline with lithium carbonate	Increased excretion of lithium carbonate
Aminophylline with propranolol	Increased theophylline serum concentrations. Antagonism of propranolol effects
Theophylline with troleandomycin or erythromycin	Increased theophylline serum concentrations
Theophylline with cimetidine	Increased theophylline serum concentrations

Drug-Food: Slo-bid™ Gyrocaps® have not been adequately studied to determine whether their bioavailability is altered when they are given with food. Available data suggest that drug administration at the time of food ingestion may influence the absorption characteristics of some or all theophylline controlled-release products resulting in serum values different from those found after administration in the fasting state.

A drug-food effect, if any, would likely have its greatest clinical significance when high theophylline serum levels are being maintained and/or when large single doses (greater than 13 mg/kg or 900 mg) of a controlled-release theophylline product are given. The influence of the type and amount of food on performance of controlled-release theophylline products is under study at this time.

Drug/Laboratory Test Interactions: When plasma levels of theophylline are measured by spectrophotometric methods, coffee, tea, cola beverages, chocolate, and acetaminophen contribute falsely high values.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential, mutagenic potential, or the effect on fertility by xanthine compounds.

Pregnancy: Pregnancy Category C.

Animal reproduction studies have not been conducted with theophylline. It is not known whether theophylline can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Theophylline should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It has been reported that theophylline distributes readily into breast milk and may cause adverse effects in the infant. Caution must be used if prescribing xanthines to a mother who is nursing, taking into account the risk-benefit of this therapy.

Pediatric Use: Safety and effectiveness in children under six years of age have not been established with this product.

ADVERSE REACTIONS: The most consistent adverse reactions are usually due to overdose and are:

Gastrointestinal: nausea, vomiting, epigastric pain, hematemesis, and diarrhea.
Central Nervous System: headaches, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, and clonic and tonic generalized convulsions.
Cardiovascular: palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, and ventricular arrhythmias.
Respiratory: tachypnea.
Renal: albuminuria, increased excretion of renal tubular cells and red blood cells, potentiation of diuresis.
Other: hyperglycemia, inappropriate ADH syndrome, and rash.

HOW SUPPLIED: Slo-bid™ Gyrocaps® 50 mg are available in bottles of 100 (NDC 0067-0057-68), bottles of 1000 (NDC 0067-0057-82) and in unit dose 10 × 10 (NDC 0067-0057-01), and are manufactured by:

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Authors are requested to furnish (in addition to the full title) a condensed title for the cover, not exceeding 60 spaces, and a running foot of not more than 35 spaces. Original articles should be accompanied by an abstract of 200 words or less, as well as up to five key words under which the paper should be indexed. Reviews, commentaries, and articles for "Experience and Reason" do not require abstracts. Authors should also supply an alphabetical list of any unusual abbreviations used and their definitions.

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References must be numbered consecutively according to their citation in the text. Abbreviations for journals should be those listed in *Index Medicus*. The following reference style (a modified form of that shown in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals") will appear in the journal effective with volume 71 (January 1983 issue):

Journal (list first three authors then et al):

1. Starzl TE, Klintmalm GBG, Porter KA, et al: Liver transplantation with use of cyclosporin A and prednisone. *N Engl J Med* 1981; 305:266–269

Book

1. Kavet J: Trends in the utilization of influenza vaccine: An examination of the implementation of public policy in the United States, in Selby P (ed): *Influenza: Virus, Vaccines, and Strategy*. New York, Academic Press Inc, 1976, pp 297–308

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Revised, July 1985

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OCTOBER 1988 VOL. 82 NO. 4

Pediatrics

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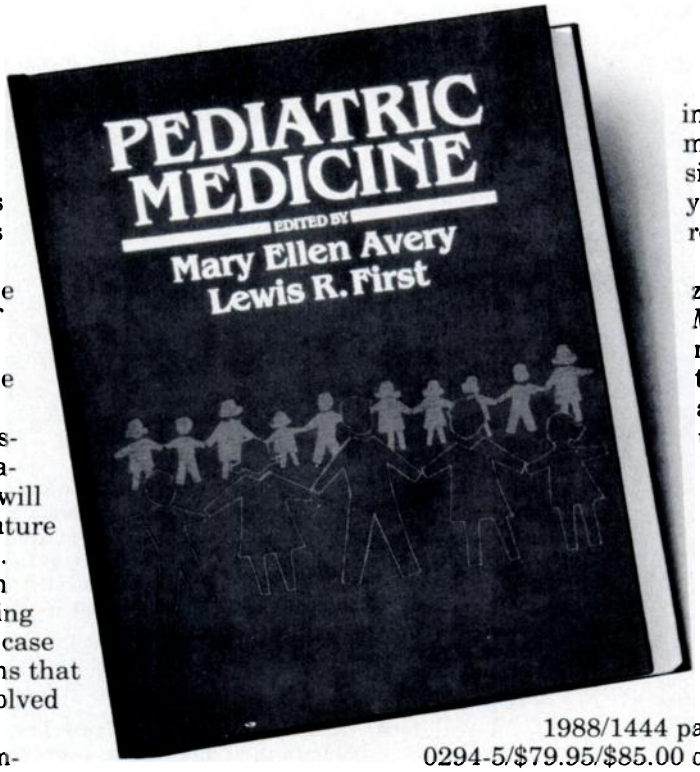

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141 Northwest Point Blvd
Elk Grove Village, IL
60009-0927

SCHEDULE OF MEETINGS

ANNUAL MEETINGS

1988
San Francisco
October 15–20

1989
Chicago
October 21–26

1990
Boston
October 6–11

1991
New Orleans
October 26–31

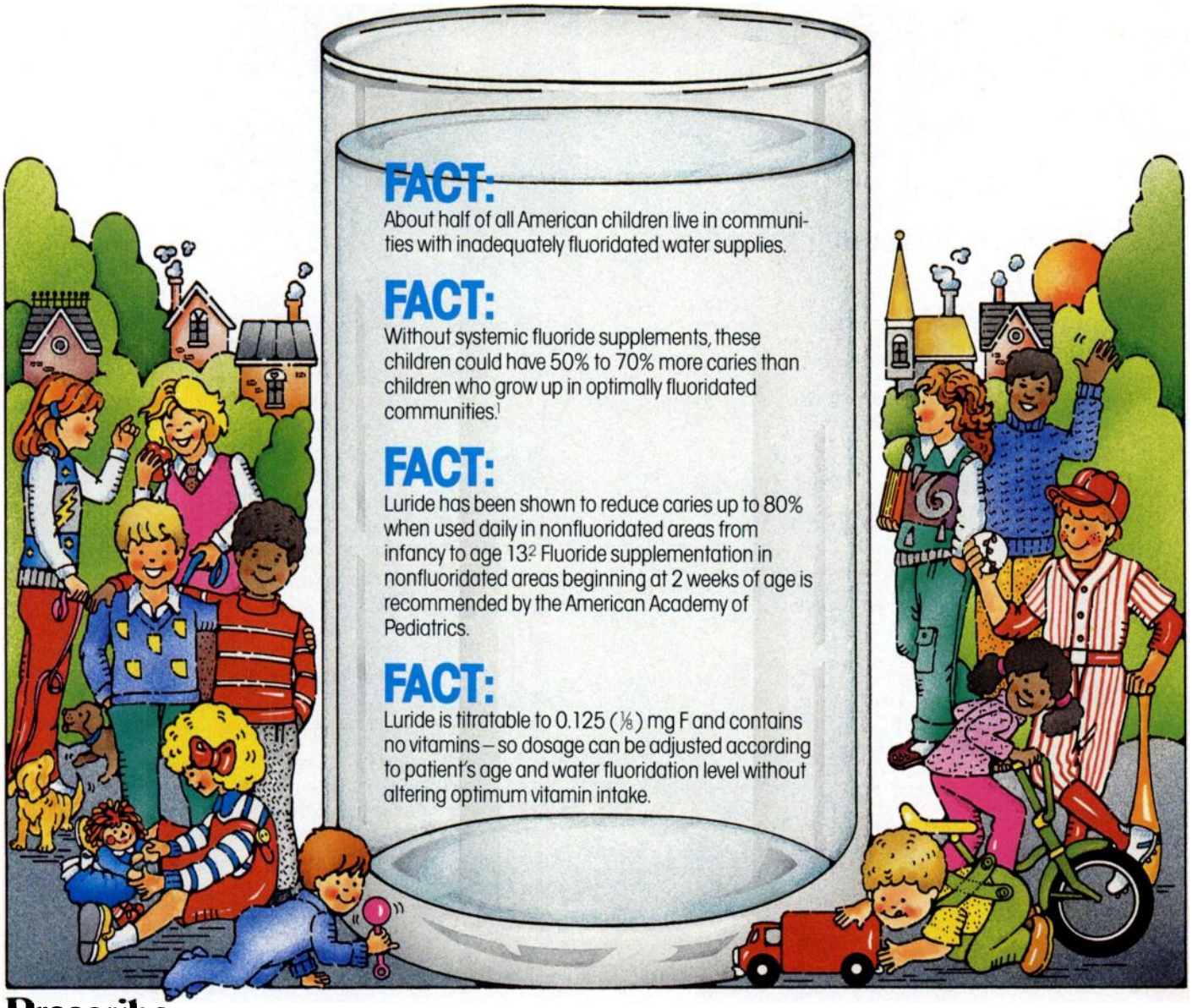
1992
San Francisco
October 10–15

SPRING SESSIONS

1989
Orlando, Florida
March 11–16

FLUORIDATED WATER.

How many of your patients live on the wrong side of the facts?



Prescribe LURIDE® Drops and Lozi-Tabs®

for babies and children who aren't getting enough fluoride from their drinking water.

Luride drops contain 0.125 (⅛) mg F per drop. Also available: Luride assorted fruit-flavored Lozi-Tabs® in doses of 0.25, 0.5, and 1.0 mg F, and Luride-SF 1 mg Lozi-Tabs with no artificial flavor or color. Luride contains no sugar or saccharin. USP quality controlled—instruct pharmacist to dispense as written.

[1]Gambowski, D. The effects of fluoridation on dental care demand. Comp. Cont. Ed. 5(8):689, 1984. [2]Aasenden, R., and T.C. Peebles. Effects of fluoride supplementation from birth on human deciduous and permanent teeth. Arch. Oral Biol. 19:321, 1978.

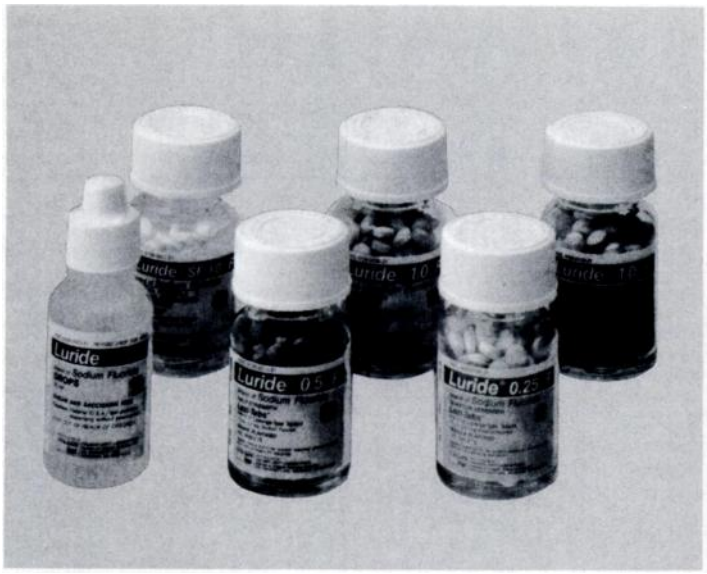
Accepted COUNCIL on DENTAL THERAPEUTICS AMERICAN DENTAL ASSOCIATION

Look for the American Dental Association Seal of Acceptance when choosing fluoride preparations.

COLGATE hoyt

Colgate-Hoyt Laboratories
Division of Colgate-Palmolive Co.
One Colgate Way · Canton, MA 02021

For complete product information and prescription pads, call Colgate-Hoyt, toll-free: 1-800-225-3756.



LURIDE® DROPS let you adjust dosage to 0.125 (⅛) mg. F.

One study showed that fluoride supplements such as Luride drops and tablets, used daily, prevented caries as effectively as fluoridated water.[1] Luride Drops and Lozi-Tabs have been shown to reduce caries up to 80% when used on a daily basis in non-fluoridated areas.[2] (Luride DMFS = 1.57, Control = 7.93)

Luride drops are sugar-free and saccharin-free, unlike many fluoride-vitamin combinations. And you can adjust dosage to the nearest 0.125 mg. F—to a single ⅛ mg. drop.

LURIDE® LOZI-TABS® TABLETS: 3 fluoride strengths, 7 child-pleasing flavors.

For children old enough to chew a tablet or let it dissolve in the mouth, Luride tablets are the logical choice. A variety of delicious fruit flavors (including our unique 4-flavor assorted package) encourages the habit of consistent, continuous use. Three strengths available—1.0 mg. F, 0.5 mg. F, and 0.25 mg. F.

LURIDE® BRAND OF SODIUM FLUORIDE DENTAL CARIES PREVENTIVE.
DESCRIPTION and HOW SUPPLIED:
All LURIDE systemic fluoride products are free of sugar and saccharin.

Product	Strength (F ION)	Package Size	Flavor
DROPS	Approx. 0.125 mg. per drop	30 ml.	peach
0.25 F TABLETS	0.25 mg. per tablet (quarter-strength)	120	vanilla
0.5 F TABLETS	0.5 mg. per tablet (half-strength)	120 1200*	grape grape
1.0 F TABLETS	1.0 mg. per tablet (full-strength)	120 1000* 5000*	cherry & assorted (cherry, orange, lemon, lime) cherry, assorted cherry
SF 1.0 F TABLETS	1.0 mg. per tablet (full-strength)	120	Special Formula, no artificial flavor or color.

*For dispensing only in quantities containing 120 mg. F. or less.
CAUTION: Federal (U.S.A.) law prohibits dispensing without prescription.

ADMINISTRATION AND DOSAGE FLEXIBILITY:
Adjustable dose LURIDE gives you the flexibility to prescribe optimal DAILY dosage (based on age and fluoride content of water).

F-Content of Drinking Water	Daily Dosage (Fluoride Ion)* Birth to Age 2	Age 2-3	Age 3-13
less than 0.3 ppm	0.25 mg. tab or 2 drops	0.5 mg. tab or 4 drops	1.0 mg. tab or 8 drops
0.3 to 0.7 ppm	one-half above dosage		
over 0.7 ppm	Fluoride dietary supplements contraindicated		

*American Dental Association, Accepted Dental Therapeutics, Edition 40 1984, page 401. American Academy of Pediatrics, Committee on Nutrition, Fluoride supplementation: revised dosage schedule. Pediatrics 63:150-152, 1979.

PRECAUTIONS: Recommended dosage should not be exceeded since prolonged overdosage may result in dental fluorosis.

REFERENCES:
(1) Arnold F.A. Jr., McClure, F.J., and White, C.L. Sodium fluoride tablets for children. D. Progress 1:8-12, 1960.

(2) Aasenden, R., and Peebles, T.C. Effects of fluoride supplementation from birth on human deciduous and permanent teeth. Arch. Oral Biol. 19:321-326, 1974; 23:111-115, 1978.

State-of-the-health day care

The new AAP Day Care Manual

The well-being of children in day care is a matter of increasing concern to parents, pediatricians, day care personnel and community health professionals.

Health in Day Care: A Manual for Health Professionals presents the latest health, safety and developmental guidelines from the American Academy of Pediatrics (AAP). This comprehensive 252-page manual discusses such important topics as:

- The role of day care in a child's development
- How to choose a good day care program
- Infections: prevention and management
- Injuries, emergencies and environmental hazards
- Child abuse
- Health training for day care personnel

Health care professionals will find authoritative answers to parents' questions about day care. And there are over 25 appendices that provide sample forms, safety checklists, guidelines for health supervision, and more.

Full Fellows of the AAP will receive one free copy of the manual upon request. Additional copies are $15, as are manuals ordered by Junior Fellows. Non-member copies are $25. Order today by returning the coupon or charge your order by calling the Academy toll free 1-800-433-9016 (in Illinois, 1-800-421-0589).

American Academy of Pediatrics

PED

Send me _____ copies of the AAP Day Care Manual, 2nd Ed. Enclosed is my check for $_____ payable to American Academy of Pediatrics. No shipping charges on prepaid orders. Mail to: AAP Publications Dept., P.O. Box 927, Elk Grove Village, IL 60009.

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Still the one and only complete line of single-food beginner foods.

1

From cereal to meats, there's still only one way to say "Introduce one single food, one at a time"—recommend the red label with "1"—BEECH-NUT® STAGES® beginner foods, a delicious selection of single-grain cereals, and single-food fruits, vegetables, meats and juices made especially for beginners. There's no lemon juice in our meats, no extra grains in our cereals. Still the one and only complete line of single-food beginner foods.

BEECH-NUT® STAGES® 1

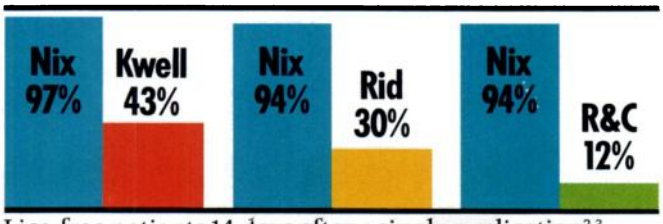
for beginners & older

Rx or OTC

The best treatment to kill lice and nits

97% effective with one application

Clinical studies prove Nix™ kills lice and nits and protects against reinfestation better than Rid,® Kwell,® or R&C Shampoo.® Only Nix provides 14-day protection against reinfestation–*with one application*–and no evidence of CNS toxicity as reported with lindane overexposure.[1]



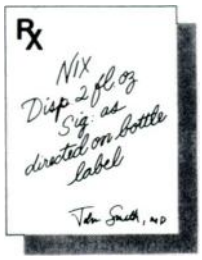
Lice-free patients 14 days after a single application.[2,3]
(Rid labelling requires a second application at 7-10 days.)

Nix® FOR LICE®
CREME RINSE
permethrin 1%

Call 1-800-FOR-LICE
to report head lice outbreaks

Please see adjacent page for brief summary of prescribing information. Wellcome

Nix FOR LICE®
CREME RINSE
permethrin 1%



PEDICULICIDAL/OVICIDAL ACTIVITIES: *In vitro* data indicate that permethrin has pediculicidal and ovicidal activity against *Pediculus humanus* var. *capitis*. The high cure rate (97-99%) of Nix in patients with head lice demonstrated at 14 days following a single application is attributable to a combination of its pediculicidal and ovicidal activities and its residual persistence on the hair which may also prevent reinfestation.

INDICATIONS AND USAGE: Nix is indicated for the single-application treatment of infestation with *Pediculus humanus* var. *capitis* (the head louse) and its nits (eggs). Retreatment for recurrences is required in less than 1% of patients since the ovicidal activity may be supplemented by residual persistence in the hair. If live lice are observed after at least seven days following the initial application, a second application can be given.

CONTRAINDICATIONS: Nix is contraindicated in patients with known hypersensitivity to any of its components, to any synthetic pyrethroid or pyrethrin, or to chrysanthemums.

WARNING: If hypersensitivity to Nix occurs, discontinue use.

PRECAUTIONS:

General: Head lice infestation is often accompanied by pruritus, erythema, and edema. Treatment with Nix may temporarily exacerbate these conditions.

Information for Patients: Patients with head lice should be advised that itching, redness, or swelling of the scalp may occur after application of Nix. If irritation persists, they should consult their physician. Nix is not irritating to the eyes; however, patients should be advised to avoid contact with eyes during application and to flush with water immediately if Nix gets in the eyes. In order to prevent accidental ingestion by children, the remaining contents of Nix should be discarded after use.

Combing of nits following treatment with Nix is not necessary for effective treatment. However, patients may do so for cosmetic or other reasons. The nits are easily combed from the hair treated with Nix after drying.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Six carcinogenicity bioassays were evaluated with permethrin, three each in rats and mice. No tumorigenicity was seen in the rat studies. However, species-specific increases in pulmonary adenomas, a common benign tumor of mice of high spontaneous background incidence, were seen in the three mouse studies. In one of these studies there was an increased incidence of pulmonary alveolar-cell carcinomas and benign liver adenomas only in female mice when permethrin was given in their food at a concentration of 5000 ppm. Mutagenicity assays, which give useful correlative data for interpreting results from carcinogenicity bioassays in rodents, were negative. Permethrin showed no evidence of mutagenic potential in a battery of *in vitro* and *in vivo* genetic toxicity studies. Permethrin did not have any adverse effect on reproductive function at a dose of 180 mg/kg/day orally in a three-generation rat study.

Pregnancy: *Teratogenic Effects:* Pregnancy Category B: Reproduction studies have been performed in mice, rats, and rabbits (200-400 mg/kg/day orally) and have revealed no evidence of impaired fertility or harm to the fetus due to permethrin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the evidence for tumorigenic potential of permethrin in animal studies, consideration should be given to discontinuing nursing temporarily or withholding the drug while the mother is nursing.

Pediatric Use: Nix is safe and effective in children two years of age and older. Safety and effectiveness in children less than two years of age have not been established.

ADVERSE REACTIONS: The most frequent adverse reaction to Nix is pruritus. This is usually a consequence of head lice infestation itself, but may be temporarily aggravated following treatment with Nix. 5.9% of patients in clinical studies experienced mild temporary itching; 3.4% experienced mild transient burning/stinging, tingling, numbness, or scalp discomfort; and 2.1% experienced mild transient erythema, edema, or rash of the scalp.

DOSAGE AND ADMINISTRATION:

Adults and Children: Nix is intended for use after the hair has been washed with shampoo, rinsed with water and towel dried. Apply a sufficient volume of Nix to saturate the hair and scalp. Nix should remain on the hair for 10 minutes before being rinsed off with water. A single treatment is sufficient to eliminate head lice infestation. Combing of nits is not required for therapeutic efficacy, but may be done for cosmetic or other reasons.

SHAKE WELL BEFORE USING.

HOW SUPPLIED: Nix (Permethrin) 1% (wt./wt.) Creme Rinse is supplied in plastic squeeze bottles that contain 2 fl. oz. weighing 56 g. (NDC-0081-0780-81)

Store at 15°-25°C (59°-77°F).

1. Davies J, Dedhia H, Morgade C, et al: Lindane poisonings, *Arch Dermatol* 1983;119:142-144.
2. Taplin D, Meinking T, Castillero P, et al: Permethrin 1% creme rinse for the treatment of *pediculus humanus* var *capitis* infestation. *Pediatr Dermatol* 1986;3:344-348.
3. Taplin D, Meinking T: Pyrethrins and pyrethroids for the treatment of scabies and pediculosis. *Semin Dermatol* 1987;6:125-135.

Burroughs Wellcome Co.
3030 Cornwallis Road
Research Triangle Park, NC 27709

Pediatric Update

December 16-18, 1988
Williamsburg Hilton
Williamsburg, Virginia

Experience the splendor of Grand Illumination Week in Colonial Williamsburg. This course is designed to give the practicing pediatrician an overview of five subspecialty areas: allergy, child development, infectious diseases, nephrology, and sports medicine.

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AMA Category I Credit: 16 Hours
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To register or for program information contact:
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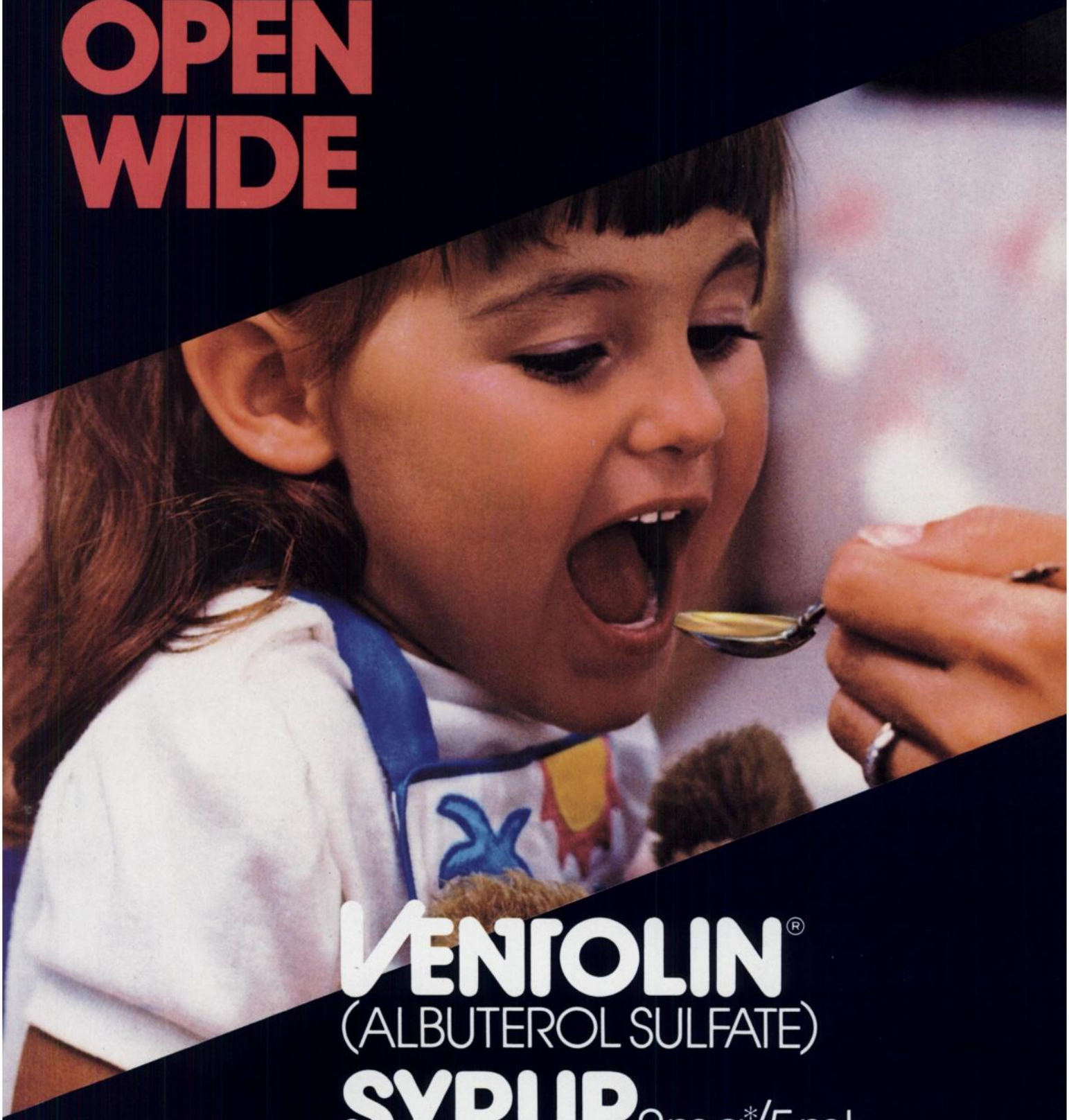
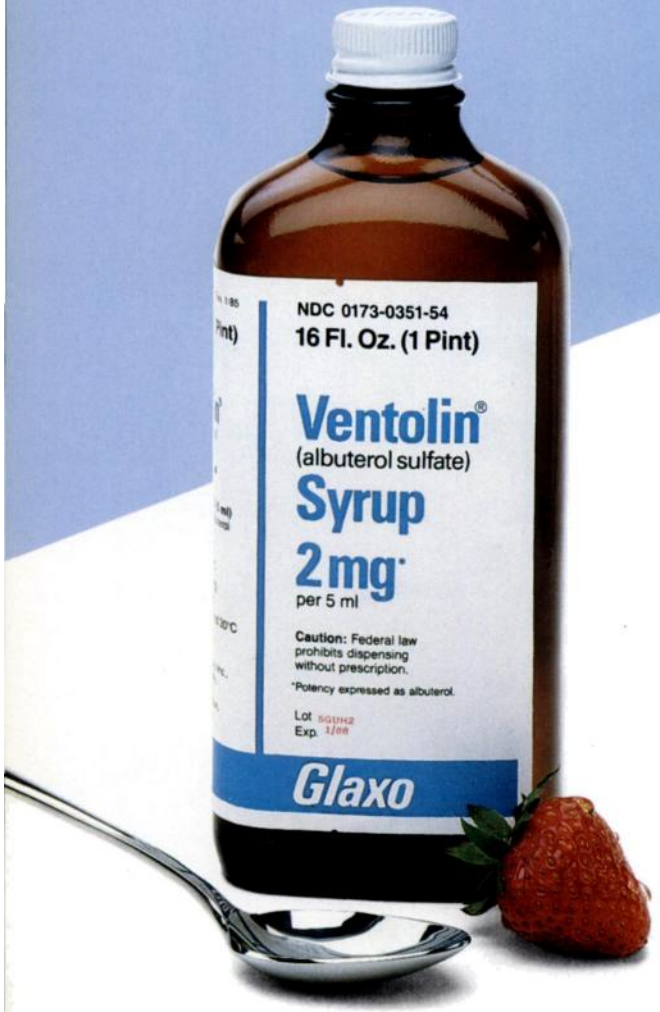


VENTOLIN®
(ALBUTEROL SULFATE)
SYRUP 2mg*/5ml

Unsurpassed bronchodilator therapy for children 2 years of age and older...flavorful taste enhances compliance...a simple t.i.d. regimen helps provide all-day and all-night control in most patients.

*Potency expressed as albuterol
Please consult next page for brief summary of Prescribing Information.

Allen & Hanburys™
DIVISION OF GLAXO INC.
a world leader in respiratory care



VENTOLIN®
(ALBUTEROL SULFATE)
SYRUP 2mg*/5ml

Unsurpassed bronchodilator therapy that goes down easy

■ Effective relief within 30 minutes...lasts as long as 6 hours

■ Promotes compliance with a flavorful taste and simple starting dosage regimen:

2 to 6 years—0.1 mg/kg body weight t.i.d. not to exceed 1 tsp (2 mg) t.i.d.
6 to 14 years—1 tsp (2 mg) t.i.d. or q.i.d.
14 years and older—1 to 2 tsp (2 to 4 mg) t.i.d. or q.i.d.

Please consult full Prescribing Information for dosage adjustment.

■ Free of undesirable additives—no sulfites, sugar, alcohol, or tartrazine (yellow dye #5)

Side effects seen with VENTOLIN Syrup in older children and adults are similar to those of other sympathomimetic agents. In children 2 to 6 years old, excitement was noted in approximately 20% and nervousness in 15%.

*Potency expressed as albuterol

VES 040R • Printed in USA • August 1988

VENTOLIN® Syrup
(albuterol sulfate/Glaxo) 2mg*/5ml

BRIEF SUMMARY

***potency expressed as albuterol**

The following is a brief summary only. Before prescribing, see complete prescribing information in VENTOLIN® Syrup product labeling.

INDICATIONS AND USAGE: VENTOLIN® Syrup is indicated for the relief of bronchospasm in adults and children 2 years of age and older with reversible obstructive airway disease.

CONTRAINDICATIONS: VENTOLIN® Syrup is contraindicated in patients with a history of hypersensitivity to any of its components.

PRECAUTIONS: General: Although albuterol *usually* has minimal effects on the beta$_2$-adrenoceptors of the cardiovascular system at the recommended dosage, *occasionally* the usual cardiovascular and CNS stimulatory effects common to all sympathomimetic agents have been seen with patients treated with albuterol, necessitating discontinuation. Therefore, albuterol should be used with caution in patients with cardiovascular disorders, including coronary insufficiency and hypertension, in patients with hyperthyroidism or diabetes mellitus, and in patients who are unusually responsive to sympathomimetic amines.

Large doses of intravenous albuterol have been reported to aggravate pre-existing diabetes mellitus and ketoacidosis. Additionally, albuterol and other beta-agonists given intravenously may cause a decrease in serum potassium, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation. The relevance of these observations to the use of VENTOLIN® Syrup is unknown.

Information for Patients: The action of VENTOLIN Syrup may last up to six hours, and therefore it should not be taken more frequently than recommended. Do not increase the dose or frequency of medication without medical consultation. If symptoms get worse, medical consultation should be sought promptly.

Drug Interactions: The concomitant use of VENTOLIN Syrup and other oral sympathomimetic agents is not recommended since such combined use may lead to deleterious cardiovascular effects. This recommendation does not preclude the judicious use of an aerosol bronchodilator of the adrenergic stimulant type in patients receiving VENTOLIN Syrup. Such concomitant use, however, should be individualized and not given on a routine basis. If regular coadministration is required, then alternative therapy should be considered.

Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants because the action of albuterol on the vascular system may be potentiated.

Beta-receptor blocking agents and albuterol inhibit the effect of each other.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Albuterol sulfate, like other agents in its class, caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium in a two-year study in the rat, at doses corresponding to 2, 9, and 46 times the maximum human (child weighing 21 kg) oral dose. In another study this effect was blocked by the coadministration of propranolol. The relevance of these findings to humans is not known. An 18-month study in mice and a lifetime study in hamsters revealed no evidence of tumorigenicity. Studies with albuterol revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Pregnancy: *Teratogenic Effects: Pregnancy Category C:* Albuterol has been shown to be teratogenic in mice when given subcutaneously in doses corresponding to 0.2 times the maximum human (child weighing 21 kg) oral dose. There are no adequate and well-controlled studies in pregnant women. Albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A reproduction study in CD-1 mice with albuterol showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg. None was observed at 0.025 mg/kg. Cleft palate also occurred in 22 of 72 (30.5%) fetuses treated with 2.5 mg/kg isoproterenol (positive control). A reproduction study in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) fetuses at 50 mg/kg, corresponding to 46 times the maximum human (child weighing 21 kg) oral dose of albuterol sulfate.

Labor and Delivery: Oral albuterol has been shown to delay preterm labor in some reports. There are presently no well-controlled studies that demonstrate that it will stop preterm labor or prevent labor at term. Therefore, cautious use of VENTOLIN® (albuterol sulfate/Glaxo) Syrup is required in pregnant patients when given for relief of bronchospasm so as to avoid interference with uterine contractility. Use in such patients should be restricted to those patients in whom the benefits clearly outweigh the risks.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children below 2 years of age have not yet been adequately demonstrated.

ADVERSE REACTIONS: The adverse reactions to albuterol are similar to other sympathomimetic agents. The most frequent adverse reactions in adults and older children were tremor (10 of 100 patients); nervousness and shakiness (9 of 100); headache (4 of 100); dizziness and increased appetite (3 of 100); hyperactivity and excitement (2 of 100); and tachycardia, epistaxis, and sleeplessness (1 of 100). The following adverse effects each occurred in less than 1 of 100 patients: muscle spasm, disturbed sleep, epigastric pain, cough, palpitations, stomachache, irritable behavior, dilated pupils, sweating, chest pain, and weakness.

In young children 2 to 6 years of age, some adverse reactions were noted more frequently than in adults and older children. These include excitement (in 20% of patients); nervousness (15%); hyperkinesia (4%); insomnia, tachycardia, and gastrointestinal symptoms (2%); and anorexia, emotional lability, pallor, fatigue, and conjunctivitis (1%).

In addition, albuterol, like other sympathomimetic agents, can cause hypertension, angina, vomiting, vertigo, central nervous system stimulation, unusual taste, and drying or irritation of the oropharynx.

The reactions are generally transient in nature, and it is usually not necessary to discontinue treatment with VENTOLIN® (albuterol sulfate/Glaxo) Syrup. In selected cases, however, dosage may be reduced temporarily; after the reaction has subsided, dosage should be increased in small increments to the optimal dosage.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

HOW SUPPLIED: VENTOLIN® Syrup, a clear, orange-yellow liquid with a strawberry flavor, contains 2 mg of albuterol as the sulfate per 5 ml in bottles of 16 fluid ounces (one pint) (NDC 0173-0351-54).

Store between 2° and 30°C (36° and 86°F).

RB2-503
July 1987

Glaxo

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When the flu upsets stomachs, make the safe call. Emetrol®

Emetrol® safely relieves nausea associated with upset stomach of intestinal flu. Morning sickness. And food indiscretions.

There are no antihistimine side effects with Emetrol®.

- No drowsiness.
- No alcohol.
- No caffeine.

Safe for children of all ages.

Emetrol® does not mask symptoms of underlying pathology. It works almost immediately by local action on contact with the hyperactive G.I. tract.

Convenient. Ideal for telephone recommendations. No Rx required.

Available in 4 and 16 oz. sizes plus the NEW 8 oz. Family Size.

BOOKS RECEIVED

Playing God, The New World of Medical Choices. T. Scully. New York, Simon & Schuster, 1988, $19.95 (HB), 431 pp.

Medical Toxicology. M J Ellenhorn and DG Barceloux. New York, Elsevier, 1987, $175 (HB), 1512 pp.

Annual Progress in Child Psychiatry and Child Development: 1987. S. Chess, A. Thomas, and M. Hertzig (eds). New York, 1988, $45, 643 pp.

Gilles De La Tourette Syndrome, ed 2. A. K. Shapiro, E. S. Shapiro, J. G. Young, et al. New York, 1988, $70, 584 pp.

Developmental and Neonatal Hematology. J. A. Stockman III and C. Pochedly (eds). New York, Raven Press, 1988, 336 pp.

Encounters With Children, Pediatric Behavior and Development. SD Dixon and MT Stein. Chicago, Year Book Medical Publishers, 448 pp.

Patterns of Birthweights. R. R. Puffer and C. V. Serrano. Washington, DC, Pan American Health Organization, 1987 (scientific publication No. 504) $10 (PB), 109 pp.

Healthy Children—Investing in the Future. US Congress, Office of Technology Assessment, OTA-H-345. Washington, DC, Government Printing Office, 1988 (Feb), $13 (PB), 301 pp.

Substance Abuse and Prevention Activities for Elementary Children. T. A. Gerne, Jr, and P. J. Gerne. Englewood Cliffs, NJ, Prentice-Hall, Inc, 1986, PB, 244 pp.

Human Gene Therapy. K. Nichols. Cambridge, MA, Harvard University Press, 1988, $22.95 (HB), $9.95 (PB), 251 pp.

Designing Clinical Research. An Epidemiologic Approach. S. B. Hulley and S. R. Cummings (eds). Baltimore, Williams & Wilkins, 1988, PB, 247 pp.

Ignatius Finds Help: A Story About Psychotherapy for Children. M. R. Galvin. New York, Brunner/Mazel Publishers, 1988, $4.95 (PB), 48 pp.

Robby Really Transforms: A Story About Grown-ups Helping Children. M. R. Galvin. New York, Brunner/Mazel Publishers, 1988, $4.95 (PB), 48 pp.

Otto Learns About His Medicine: A Story About Medication for Hyperactive Children. M. R. Galvin. New York, Brunner/Mazel Publishers, 1988, $4.95 (PB), 32 pp.

This Is Me and My Two Families. M. D. Evans. New York, Magination Press, 1986, $12.95 (PB), 87 pp.

PEDIATRICS IN REVIEW: December 1988 Contents

A grape new way to help raise compliance!

New Grape Flavor
CHILDREN'S
TYLENOL®
acetaminophen
ELIXIR

First choice for fever and pain relief

Now...a choice of two great-tasting elixirs to promote even better dosage compliance

Because children often prefer one flavor over another, TYLENOL® offers them a choice: New Grape joins original Cherry Elixir to help improve acceptance and encourage compliance.[1] And, as you know, better compliance helps assure optimal efficacy.

Proven equally effective as aspirin for fever and pain relief[2,3] with a superior safety profile,[4] alcohol-free Children's TYLENOL® Elixirs come with a calibrated dosage cup for easy, accurate administration.

To help raise patient compliance in your practice, recommend the only brand that offers two elixir flavors—Children's TYLENOL®.

References: 1. Data on file, McNeil Consumer Products Company. 2. Tarlin L, et al: *Am J Dis Child* 1972;124:880-882. 3. Cooper SA: *Arch Intern Med* 1981;141:282-285. 4. Aspirin or paracetamol? *Lancet* 1981;II:287-289.

McNeil Consumer Products Company
Fort Washington, PA 19034
McNEIL

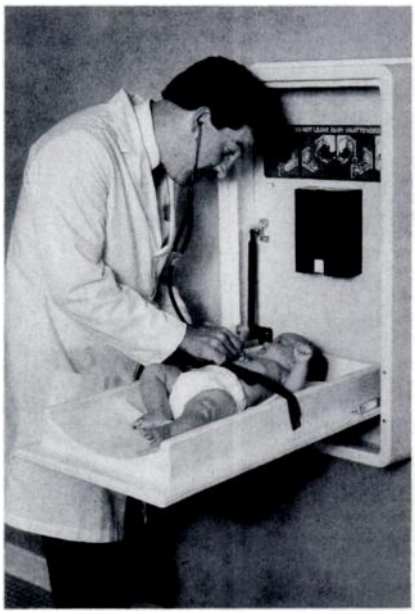
If Infant Exams Frustrate You, Examine This.

At last, there's an affordable, thoughtfully designed examination table that eliminates the frustrations of infant exams: the Koala Bear Kare Baby Changing Station.

The device was originally created as a safe, convenient diaper changing facility for public restrooms. But in early 1988, a physician in Muskegon, Michigan, noticed the Changing Station in a restaurant restroom and realized that the fixture would make an excellent infant exam table. Since then, Changing Stations have been installed as exam tables in a number of pediatric offices, family practice offices and clinics.

The Changing Station offers you several significant benefits:

—Easier Exams. The concave surface and sturdy safety straps keep active infants securely in place, allowing you to perform more thorough exams.



—Unassisted Exams. Because the station's unique design prevents infants from rolling or crawling away, you can examine tiny patients without an assistant.

—A Sanitary Surface. Disposable liners keep the examination surface clean.

—Efficient Use Of Space. The station mounts on the wall and folds away when not in use.

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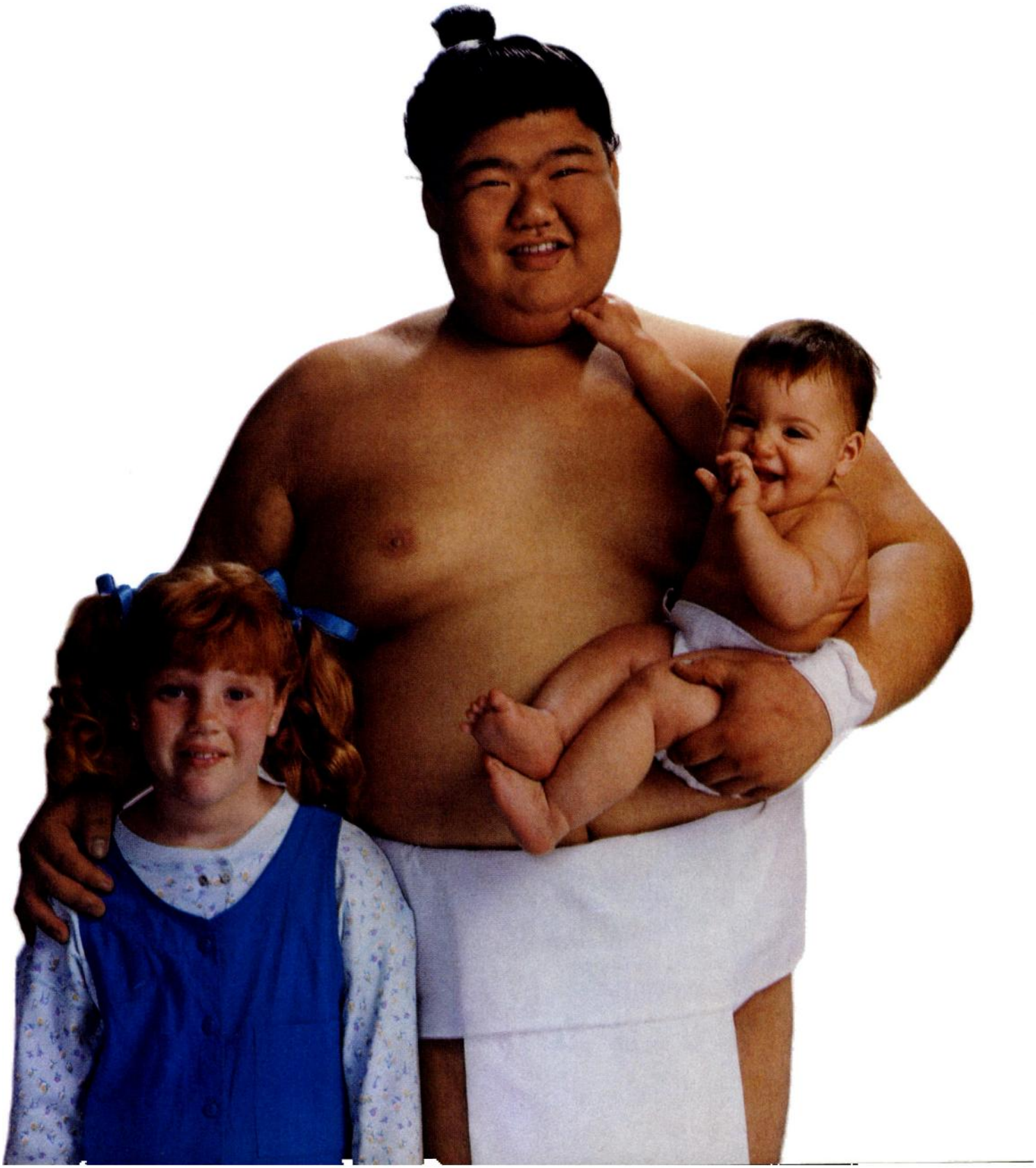
For all the ways infant gas

In steroid-responsive dermatoses

A firm but gentle touch



UNIQUE, NONFLUORINATED

AcloVATE®

(alclometasone dipropionate)

CREAM, 0.05% OINTMENT, 0.05%

For kids of all sizes

Significantly outperforms Hytone, 1.0%[1]

Some dermatoses need a firm hand. ACLOVATE Cream, 0.05% proved significantly more effective than Hytone®* (hydrocortisone) Cream, 1.0% in atopic dermatitis.[1] Multipurpose ACLOVATE is effective and well tolerated in a broad range of steroid-responsive dermatoses,[1-4] including diaper dermatitis.[2†] Furthermore, in psoriasis, ACLOVATE Ointment, 0.05% compares favorably with Tridesilon®‡ (desonide) Creme, 0.05% and Ointment, 0.05%.[1]

Safety comparable to hydrocortisone, 1.0%

ACLOVATE provides patients with the gentleness of a low-potency steroid and a safety profile comparable to hydrocortisone, 1.0%.[1] In a study of 39 children, aged 3 months to 12 years, there were no reports of local or systemic adverse effects with ACLOVATE.[2]

Not available over the counter

Multipurpose ACLOVATE is a unique, nonfluorinated steroid molecule and is not available over the counter. ACLOVATE is available in 15 g and 45 g tubes.

*Registered trademark of Dermik Laboratories, Inc.
†As with all topical corticosteroids, caution should be exercised when prescribing ACLOVATE for pediatric use because of a greater susceptibility to HPA axis suppression in children than in mature patients.
‡Registered trademark of Miles Inc., Pharmaceutical Division.

REFERENCES: 1. Data available on request, Glaxo Inc. **2.** Crespi HG: Topical corticosteroid therapy for children: alclometasone dipropionate cream 0.05%. *Clin Ther* 1986;8(2):203-210. **3.** Lassus A: Clinical comparison of alclometasone dipropionate cream 0.05% with hydrocortisone butyrate cream 0.1% in the treatment of atopic dermatitis in children. *J Int Med Res* 1983;11:315-319. **4.** Kint A: Treatment of atopic dermatitis in children: alclometasone dipropionate cream 0.05% versus hydrocortisone butyrate cream 0.1%. *Acta Ther* 1987;13:455-466.

Please see Brief Summary of Prescribing Information on following page.

Glaxo Dermatology Products
Division of Glaxo Inc.
Research Triangle Park, NC 27709
Unique compounds advancing dermatology

ACL056 Printed in USA August 1988

ACLOVATE®
(alclometasone dipropionate)

CREAM, 0.05% OINTMENT, 0.05%

BRIEF SUMMARY

For Dermatologic Use Only — Not for Ophthalmic Use.

The following is a brief summary only. Before prescribing, see complete prescribing information in ACLOVATE® Cream and Ointment product labeling.

CONTRAINDICATIONS: ACLOVATE® Cream and Ointment are contraindicated in patients who are hypersensitive to alclometasone dipropionate, to other corticosteroids, or to any ingredient in these preparations.

PRECAUTIONS: General: Systemic absorption of topical corticosteroids has resulted in reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions that augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (see PRECAUTIONS: Pediatric Use).

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatologic infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Information for Patients: Patients using ACLOVATE® should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions, especially under occlusive dressing.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests: Although ACLOVATE® Cream and Ointment were shown not to produce HPA axis suppression, the following tests may be helpful in evaluating if HPA axis suppression does occur.

Urinary free cortisol test

ACTH stimulation test

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids.

Studies to determine mutagenicity with prednisolone have revealed negative results.

Pregnancy: *Teratogenic Effects: Pregnancy Category C:* Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic in animals after dermal application.

There are no adequate and well-controlled studies of the teratogenic effects of topically applied corticosteroids in pregnant women. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities not likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are prescribed for a nursing woman.

Pediatric Use: Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS: The following local adverse reactions have been reported with ACLOVATE® Cream: itching occurred in about 2 per 100 patients; burning, erythema, dryness, irritation, and papular rashes occurred in about 1 per 100 patients.

The following local adverse reactions have been reported with ACLOVATE® Ointment: itching or burning, 1 per 200 patients; and erythema, 2 per 1,000 patients.

The following local adverse reactions have been reported with topical dermatologic corticosteroids, especially under occlusive dressings: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infections, skin atrophy, striae, and miliaria.

OVERDOSAGE: Topically applied ACLOVATE® can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS).

Glaxo

April 1988

Glaxo Dermatology Products
Glaxo Inc
Research Triangle Park, NC 27709

Manufactured for Glaxo Inc., Research Triangle Park, NC 27709
by Faltering Corporation, Kenilworth, NJ 07033

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Benadryl®
Decongestant Elixir
For nasal decongestant action in colds

Pediatric patients with congested colds will welcome the effects of Benadryl® Decongestant Elixir—"The Unstuffer." It effectively opens clogged sinus and nasal passages so children with colds or upper respiratory allergies can breathe more easily. You can rely on Benadryl® Decongestant Elixir just as physicians have relied on Benadryl® Elixir for decades. Both have a place in your practice.

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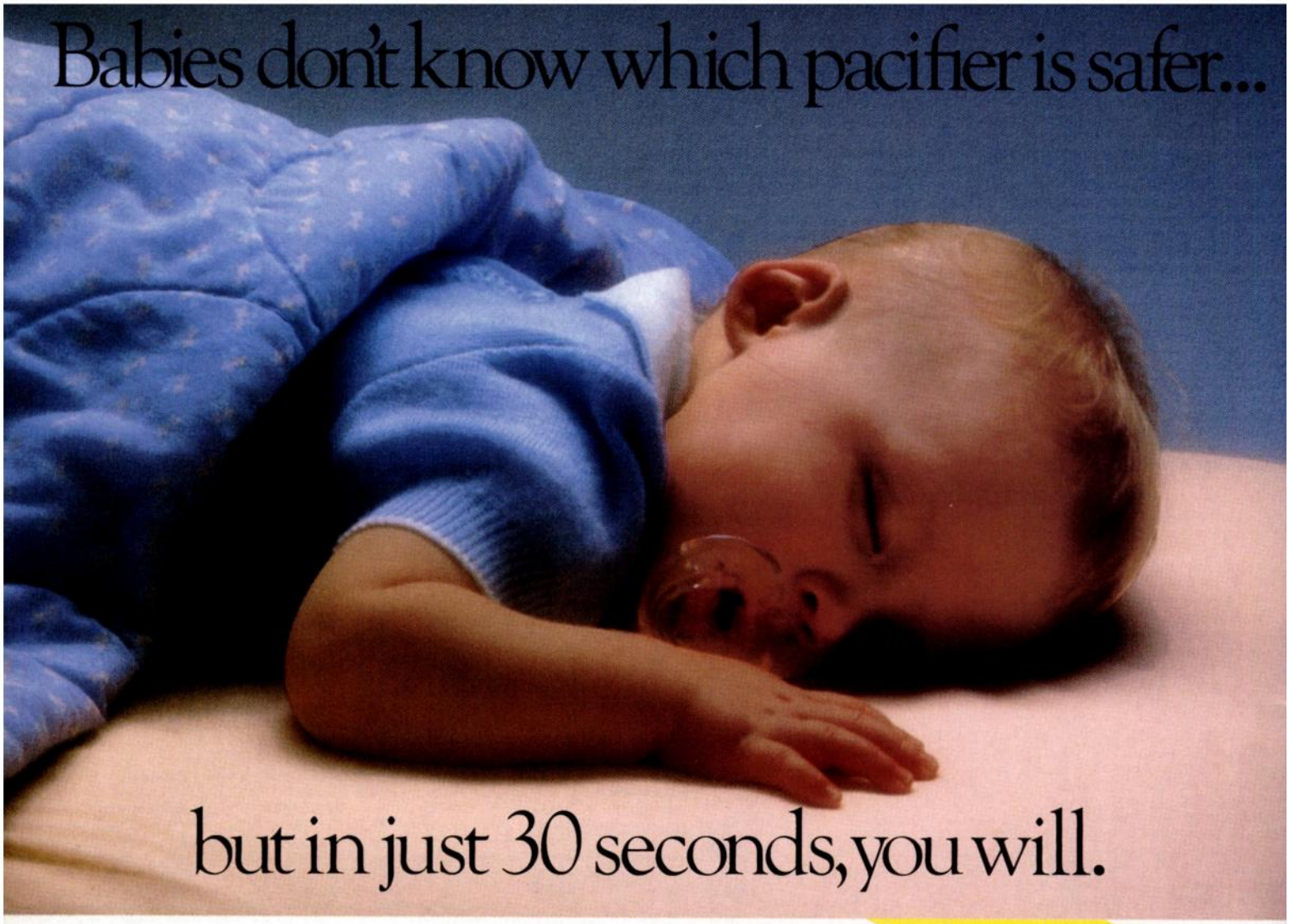
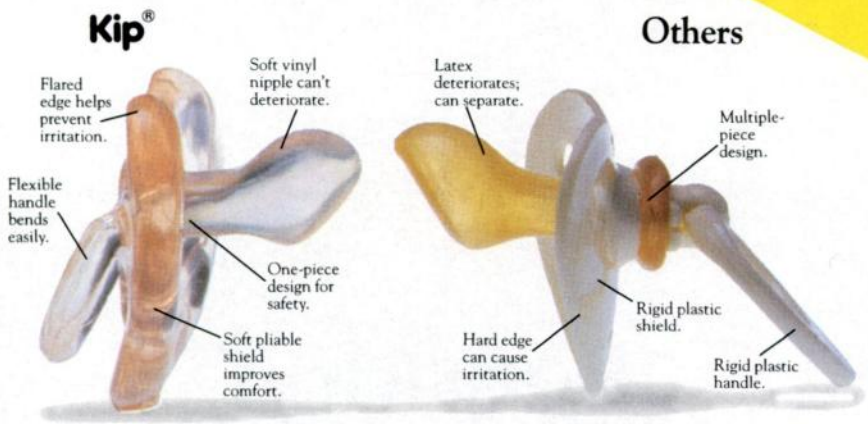
P1275(2-87)

Babies don't know which pacifier is safer...



but in just 30 seconds, you will.



Come see us at AAP's 57th Annual Meeting, San Francisco, Oct. 15-20, Booth #434

You probably know that your baby's urge to suck is a natural instinct that feeding alone may not satisfy. That's why pacifiers may be appropriate for your child.

But are you aware that many pacifiers have built-in safety hazards? Including some of the most popular brands?

The First Years® puts safety first.

The First Years pacifier was designed for infant safety and reviewed for overall appeal by a maternity hospital and members of our unique Mothers' Council. Both enthusiastically approved it. The result is Kip, a safe, reliable pacifier you can trust.

Kip vs. the competition.

Many popular pacifier nipples are made of latex. Because saliva breaks down latex, they warn you to test the nipple each time it's used, to make sure it won't separate and become a choking hazard.

Our Kip is one-piece, super-soft vinyl that's 100% nitrosamine-free. It will never deteriorate or come apart. And, as you can see, it has many other features that help take the worry out of quiet time.

Get to know our family.

Kip and our exclusive Newborn Kip (just right for smaller newborn mouths) are just two of the over 200 thoughtfully-designed, mother-tested products we make that naturally complement the loving care you give. Look for them in major discount, drug, grocery and toy stores everywhere. Or call *toll-free* 1-800-533-6708 for a store listing.

the first years®

Carnation® introduces

A BREAKTHROUGH HYPOALLERGENIC INFANT FORMULA

Introducing

THE FIRST HYPOALLERGENIC FORMULA MADE FROM HYDROLYZED WHEY PROTEIN

Available in easy-to-dissolve powder, in 12-oz cans.

Because of increasing recognition of the sensitivity to soy,[1] Carnation has developed the first truly hypoallergenic formula made from hydrolyzed whey protein.

Carnation® GOOD START H.A. effectively resolves symptoms in infants suffering from formula intolerance or milk allergy. And, it may prevent allergic manifestations in infants with a family history of allergy.

No curd formation and rapid gastric emptying, similar to breast-fed infants, make GOOD START H.A. easy to digest. Because of its whey base, it's a high-quality protein source for optimal growth. Parents will like its pleasant taste and aroma. And, it's moderately priced for long-term use.

The GOOD START H.A. formulation has been thoroughly researched in clinical trials and safely fed to more than 25,000 infants over the past 3 years in Europe.

Low Allergic Reaction Rates With GOOD START H.A.™

In five studies of 417 infants from atopic families, only one study showed a 3.6% reaction rate, while the other four studies showed 0% reaction rates with the GOOD START H.A. hypoallergenic formulation.[2-6]

Carnation®

New **GOOD START H.A.**™

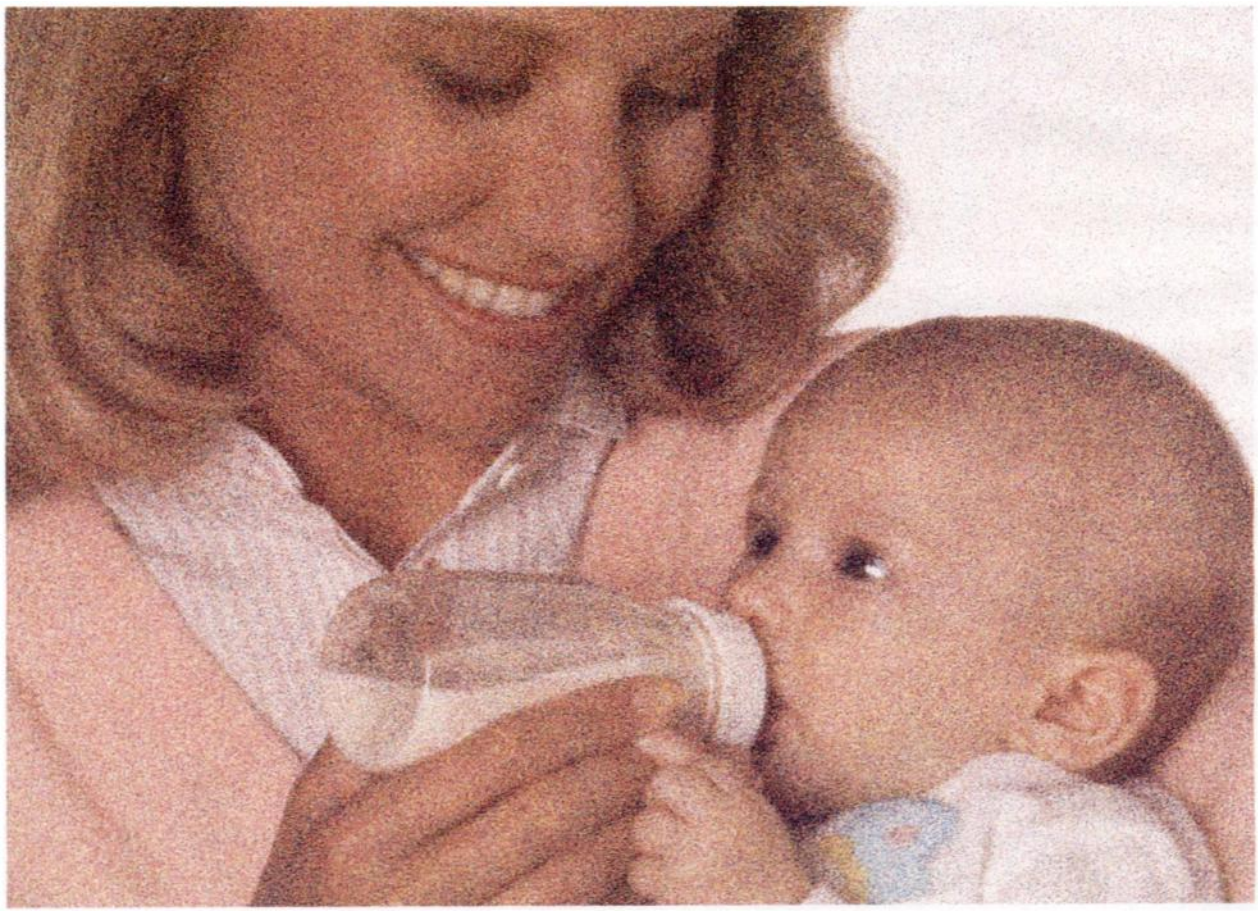
Hypoallergenic Infant Formula

. . . a change for the better

INSTEAD OF SOY, CHANGE TO NEW GOOD START H.A.™

Sensitivity to soy increasingly recognized[1]

About one fourth of infants who are sensitive to cow's milk protein are also intolerant of soy protein.[7,8]



Recommend GOOD START H.A.™ for:

Formula Intolerance, Instead of Soy

Resolves symptoms of milk allergy or intolerance such as spitting up, skin rash, runny nose, and colic

Routine Feeding of Atopic Infants

May prevent allergic manifestations in infants with a family history of allergy[2]

Routine Feeding of Normal Infants

Nutritionally complete for optimal growth and development

REFERENCES:

1. Committee on Nutrition, American Academy of Pediatrics: *Pediatric Nutrition Handbook*, ed 2, Forbes GB, Woodruff CW (eds). Elk Grove Village, Ill, American Academy of Pediatrics, 1985, p 210.

2. Vandenplas Y, Deneyer M, Sacre L, et al: Preliminary data on a field study with a new hypo-allergic formula. *Eur J Pediatr*, to be published.

3. Kahn A, Rebuffat E, Blum D, et al: Difficulty in initiating and maintaining sleep associated with cow's milk allergy in infants. *Sleep* 1987;10:116-121.

4. Zabransky S, Zabransky M: Preliminary clinical experience with a hypoallergenic infant formula. *Extracta Paediatrica* 1987;11:10-12.

5. Schmidt E, Reinhardt D, Gerke R: The use of hypoallergenic milk formulas in newborns. *Der Kinderarzt* 1987;5:627-631.

6. Denis R, Willeme D: Data on file, Carnation Co.

7. Bahna SL, Heiner DC: *Allergies to Milk*. New York, Grune & Stratton, 1980, p 127.

8. Gerrard JW, Lubos MC, Hardy LW, et al: Milk allergy: Clinical picture and familial incidence. *Can Med Assoc J* 1967;97:780-785.

Carnation®

New **GOOD START H.A.™**

Hypoallergenic Infant Formula

. . . a change for the better

Carnation®

GOOD START H.A.™

Hypoallergenic Infant Formula

A CHANGE FOR THE BETTER

Nutritionally close to breast milk

Amino acid balance close to breast milk

The added fat blend is 100% vegetable oil, high in monounsaturates:

GOOD START H.A.—44.5% of the fatty acid component is monounsaturated
Breast milk—40.2% of the fatty acid component is monounsaturated

Polyunsaturated-to-saturated ratio is similar to breast milk:
GOOD START H.A. P/S ratio = 0.31
Breast milk P/S ratio = 0.28–0.35*

Carbohydrate content is 70% lactose (the *only* carbohydrate in breast milk), for better absorption of calcium, magnesium, and zinc:

30% of the carbohydrate content is maltodextrin, which is easily digested and helps keep osmolarity low to protect against osmotic diarrhea

NOTE: GOOD START H.A. should not be used for infants with galactosemia.
*Varies with individual.

Carnation®

Nutrition that tastes good.™

Information for Healthcare Professionals

Carnation®

GOOD START H.A.™

Hypoallergenic Infant Formula

Introduction to GOOD START H.A.™

Cow's milk intolerance is relatively common in infants[1,2] and soy protein intolerance is becoming increasingly recognized.[3,4] GOOD START H.A. was developed to meet the needs of infants with intolerance to either protein source.

The hypoallergenicity of GOOD START H.A. is effected by heat treatment and enzyme hydrolysis of whey protein. This process alters the protein structure and size, which reduces the potentially allergenic whey protein to controlled-length peptides, while still preserving the nutritional qualities of whey. The average peptide length is only 5.6 amino acids, with an average molecular weight of 638 daltons. By contrast, soy protein is a mixture of variously sized protein chains that range in weight from 8,000 to 600,000 daltons.[5]

Small peptide size is indicative of low potential for allergenicity, but it is not an absolute indicator. Therefore, Carnation has verified the hypoallergenicity of the GOOD START H.A. formulation by use of animal sensitization and challenge tests and highly sensitive radioimmunoassays to identify specific antigens.[6]

Each batch of GOOD START H.A. infant formula is evaluated for hypoallergenicity by electrophoresis and double immunodiffusion to assure that the peptide profile is hypoallergenic. Before processing, the whey protein source contains 12% potentially allergenic material. In GOOD START H.A., the maximum allowed per batch is less than 0.1%.

The following general summary includes the nutritional profile of GOOD START H.A. and an overview of the major clinical studies.

GOOD START H.A. is available, as an easy-to-dissolve powder, in 12-oz cans.

The Nutritional Profile of GOOD START H.A.™

GOOD START H.A. is nutritionally complete for routine infant feeding. Its hypoallergenicity and sensory characteristics make it an appropriate dietary regimen to resolve symptoms of formula intolerance and to prevent symptoms in infants at high risk due to family history of allergy.

The energy distribution in GOOD START H.A. infant formula is very similar to that in breast milk; 9.8% of total energy is derived from protein, 46% from fat, and 44.2% from carbohydrate.

Protein

One hundred percent of the protein in GOOD START H.A. comes from whey which is high in essential amino acids, and is a higher quality protein than soy- or casein. The amino acid profile of GOOD START H.A. is close to that of breast milk.

The hypoallergenicity of GOOD START H.A. is created by heat treatment and enzyme modification of whey protein, and is verified in animal challenge studies and radioimmunoassays of the formulation.

Because the heating time required in the production of GOOD START H.A. is very short, the formula retains milk-like attributes in appearance, taste, and aroma. No curd formation and rapid gastric emptying, similar to that of breast-fed infants, make GOOD START H.A. easy to digest.

Fat

The 100% vegetable fat blend in GOOD START H.A. is composed of 60% palm olein, 22% high-oleic safflower oil, and 18% coconut oil. Only the high *oleic* varieties of palm and safflower oil, which are high in monounsaturated fatty acids, are added to GOOD START H.A. The polyunsaturated-to-saturated fat ratio in GOOD START H.A. is 0.31, close to the range found in breast milk, which is approximately 0.28. When reconstituted, the fat content of GOOD START H.A. (3.7 g/100 mL) is close to the average fat content in breast milk (3.8 g/100 mL).

Carbohydrate

The carbohydrate content of GOOD START H.A. formula is 70% lactose and 30% maltodextrin. The lactose component of the hydrolyzed whey is retained because it is the carbohydrate of breast milk, and it promotes absorption of important minerals, especially calcium, magnesium, and zinc. This is important for long-term and routine feeding. The addition of maltodextrin (complex carbohydrate) to GOOD START H.A. helps maintain low osmolarity to protect against osmotic diarrhea.

New information is emerging about lactose in diets of infants with diarrhea. In one study,[7] 40 infants with chronic diarrhea and soy intolerance were given formulas containing one of three carbohydrate sources. Improvement in stool frequency and volume was observed in 86% of the infants who received the formula containing lactose, compared with 20% and 19% who improved in the group fed formulas containing maltodextrin or sucrose, respectively. In the same study, no improvement had been noted with a lactose-free hydrolyzed casein formula. Another study[8] assessed the difference in recovery times in 85 infants with mild acute gastroenteritis (more than six watery stools per day for 1 week or longer) who received formulas with lactose, sucrose, polycose, or sucrose/polycose as the carbohydrate source. Results showed most infants recovered from mild gastroenteritis irrespective of the carbohydrate ingested.

The American Academy of Pediatrics Committee on Nutrition[9] summarizes the situation. In discussing the treatment of enteritis the AAP states, **"The current data do not suggest that lactose should be routinely eliminated from the diet of infants recovering from diarrhea, although some experienced clinicians make this recommendation."**

Infants with galactosemia, a rare congenital condition, should not be given lactose-containing formulas.

Vitamins and Minerals

GOOD START H.A.™ Hypoallergenic Infant Formula includes all known necessary vitamins in conformance with the recommendations of the Committee on Nutrition of the American Academy of Pediatrics. Unlike soy formulas, GOOD START H.A. contains no phytates, which can inhibit absorption of iron, copper, and zinc.

The major minerals and important nutrient ratios of GOOD START H.A. and breast milk are shown in the Table below.

Table. Major Minerals and Important Nutrient Ratios: GOOD START H.A. and Breast Milk

Mineral	GOOD START H.A., mg/100 mL	Breast Milk, mg/100 mL
Sodium	16.0	15.0
Potassium	66.0	60.0
Chloride	39.0	43.0
Calcium	43.0	35.0
Phosphorus	24.0	15.0
Magnesium	4.5	2.8
Iron	1.0	*
	Ratios	
Ca/P	1.8	2.3
Na/K	0.41	0.42
Na+K/Cl	2.05	2.0

*Variable and difficult to measure; usually low content, but with high bioavailability.

Other Characteristics of GOOD START H.A.™

The osmolality of GOOD START H.A. is typically 265 mosm/kg water compared with 300 mosm/kg water for breast milk. The renal solute load (100.6 mosm/L) is also similar to that of breast milk (79 mosm/L).

The pleasant taste, appearance, and aroma of GOOD START H.A. may enhance parental compliance.

A practical advantage of GOOD START H.A. is that the powder dissolves quickly and completely in warm water.

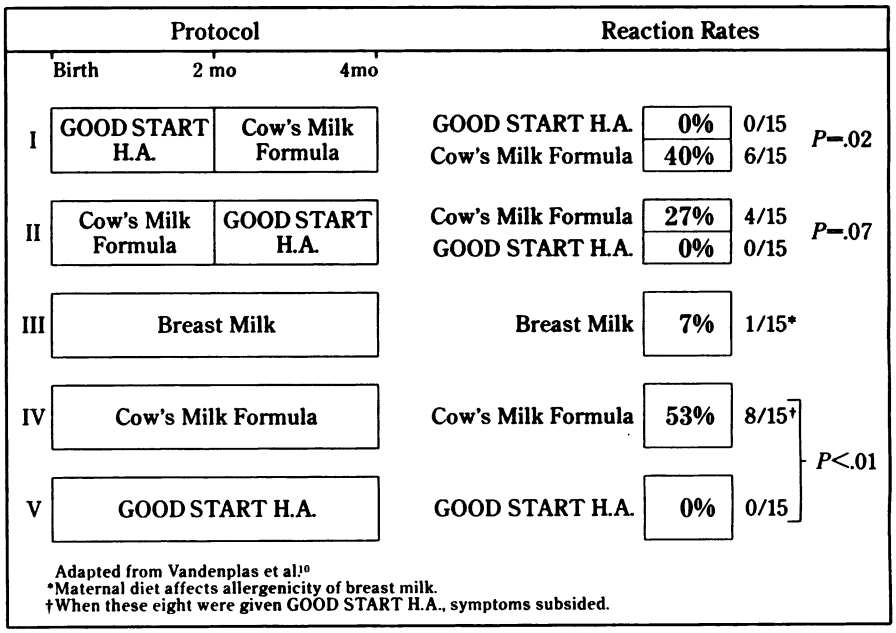
CLINICAL STUDIES OF GOOD START H.A.™

Clinical studies of the GOOD START H.A. formulation show:

- Symptoms of intolerance to cow's milk formulas are resolved[10]
- In infants at high risk of allergy due to family history, atopic symptoms of allergy occur far less frequently[10] than the published incidences of symptoms with cow's milk or soy-based formulas[1,3,11]
- Optimal growth and development
- Stools are similar to those of breast-fed infants

Prevention of Atopy in High-Risk Infants

Seventy-five infants with one or both atopic parents or siblings were included in a study by Vandenplas et al.[10] *Figure 1* indicates the nutritional feeding protocol given to the five groups of infants for the first 4 months and the number of infants with allergic symptoms. No infants had atopic symptoms while being fed GOOD START H.A. This included the group of four infants that had atopic symptoms from a 2-month cow's milk formula protocol before switching to the GOOD START H.A. protocol. Because six infants who previously had no reactions while being fed GOOD START H.A. subsequently had reactions to cow's milk formula, the investigators conclude that the GOOD START H.A. formulation both resolves and may prevent the appearance of allergic symptoms in atopic infants.



Adapted from Vandenplas et al.[10]
*Maternal diet affects allergenicity of breast milk.
†When these eight were given GOOD START H.A., symptoms subsided.

Figure 1. Comparison of allergic reaction rates in infants at risk of food allergy due to family history (N=75).[10]

Lack of Sensitization in Atopic Infants

Because brief exposure of an atopic infant to cow's milk can sensitize the infant to milk, Schmidt et al[12] evaluated three different feeding phases in a study of 45 infants at high risk of allergy due to positive family histories: (1) supplementation with the GOOD START H.A. formulation in the nursery until full lactation was achieved (from birth to approximately day 5 of life); breast-feeding for the first 4 to 6 months; (2) GOOD START H.A. reintroduced and breast-feeding discontinued for at least 1 month; (3) switch to cow's milk formula following GOOD START H.A. (under clinical supervision) at 6 to 7 months of age.

When the GOOD START H.A. formulation was reintroduced after discontinuation of breast-feeding, there were no noticeable signs of intolerance or allergy as would have been expected with cow's milk formula in these atopic infants. In fact, when the infants were switched to the cow's milk formula following GOOD START H.A., three had symptoms after the first feeding (two had slight transient erythema; one had diarrhea) *(Fig 2)*.

Forty-five Infants During Three Feeding Phases

	PHASE I	PHASE II	PHASE III
Feeding	**BREAST MILK** (GOOD START H.A. used as supplement first 5 days)	**GOOD START H.A.**	**COW'S MILK FORMULA**
Duration	4–6 months	1 month	1 month
Age	Birth to 4–6 months	4–6 months	6–7 months
No. of infants with symptoms	0	0	3 (2 transient erythema;* 1 diarrhea)

Figure 2. Results of switching to GOOD START H.A. after breast-feeding, then switching to cow's milk formula. (N=45 "at-risk" newborns).[12]

*May be due to maternal intake of cow's milk protein.

Resolution of Allergy Symptoms

Kahn et al[13] studied the sleeping patterns of 71 infants fed either GOOD START H.A. or cow's milk formula. The infants were put into four groups: (I) 20 with insomnia and suspected cow's milk allergy; (IIa) 18 infants who were "poor sleepers" and had skin and gastrointestinal symptoms attributed to cow's milk allergy; (IIb) 13 infants with skin and gastrointestinal symptoms and normal sleep patterns; and (III) 20 normal controls—infants with neither symptoms of allergy nor sleep disruption.

After 4 weeks of feeding, those fed with the GOOD START H.A. formulation slept much longer than those fed cow's milk formula. The duration of sleep in Groups I and II, fed GOOD START H.A., almost increased to the equivalent sleep time of the control group *(Fig 3)*.

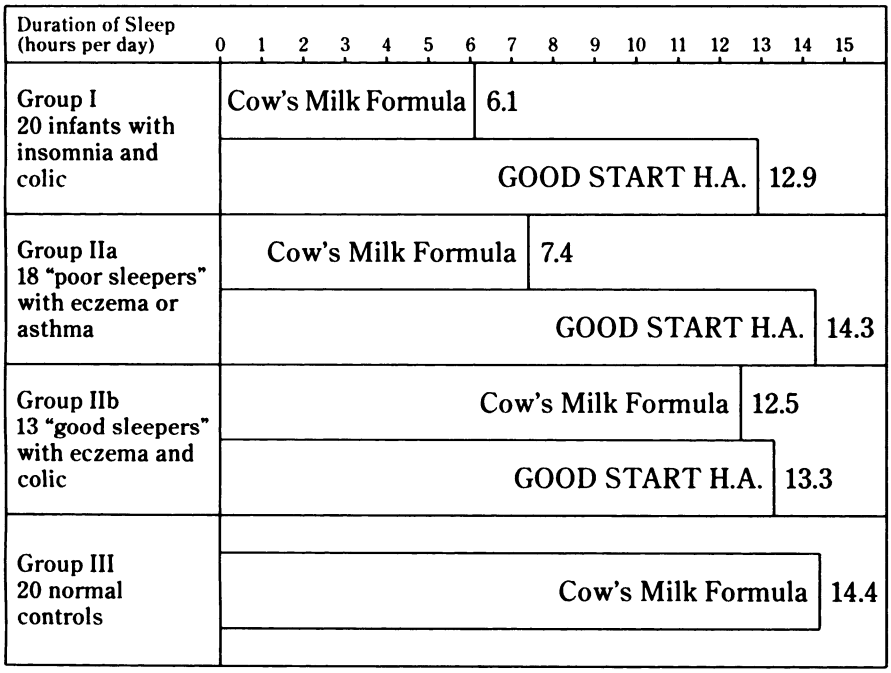


Figure 3. Comparison of sleep patterns when infants were fed GOOD START H.A. vs. cow's milk formula.[13]

Complement to Breast-feeding

Zabransky and Zabransky[14] studied 162 healthy, mature newborn infants who received the GOOD START H.A. formulation as a supplement in the nursery for several days until breast-feeding was established. The infants readily accepted GOOD START H.A., and their weight development was reported to be better than when glucose solutions were used to supplement breast-feeding during the first days. GOOD START H.A. was continued as a complement to breast-feeding for 53 of the infants because they had family histories of allergy. No allergic reactions were seen.

In another study, Passian[15] evaluated 91 infants who were only breast-fed or breast-fed and fed GOOD START H.A. (47) or who received only the GOOD START H.A. formulation (44). Weight progression during the first six days of life was similar in the two groups. Stools of the infants who received GOOD START H.A. were soft to watery, as if breast-fed exclusively.

GOOD START H.A.™

Hypoallergenic Infant Formula

Complete Nutritional Information

INGREDIENTS: 42% ENZYMATICALLY HYDROLYZED REDUCED MINERALS WHEY AND WHEY PROTEIN CONCENTRATE, 24% VEGETABLE OILS (PALM OLEIN, HIGH-OLEIC SAFFLOWER AND COCONUT), 17% MALTODEXTRIN, 14% LACTOSE, 1% LECITHIN, AND LESS THAN 1% OF EACH OF THE FOLLOWING: CALCIUM CHLORIDE, POTASSIUM CHLORIDE, POTASSIUM CITRATE, CALCIUM PHOSPHATE, CHOLINE BITARTRATE, SODIUM ASCORBATE (VITAMIN C), SALT, MAGNESIUM CHLORIDE, TAURINE, FERROUS SULFATE (IRON), INOSITOL, ZINC SULFATE, L-CARNITINE, ALPHA TOCOPHERYL ACETATE (VITAMIN E), NIACINAMIDE, CALCIUM PANTOTHENATE, COPPER SULFATE, RIBOFLAVIN, VITAMIN A ACETATE, PYRIDOXINE HYDROCHLORIDE (VITAMIN B6), THIAMINE MONONITRATE, FOLIC ACID, PHYLLOQUINONE (VITAMIN K), POTASSIUM IODIDE, VITAMIN D3, MANGANESE SULFATE, BIOTIN, VITAMIN B12.

NOTE: CONTAINS LACTOSE

5 FL OZ PROVIDES 100 CALORIES, PREPARED AS DIRECTED.

	Per 100 Calories		Caloric Distribution
NUTRIENTS:			
PROTEIN	2.4	g	9.8%
FAT	5.1	g	46.0%
CARBOHYDRATE	11	g	44.2%
WATER	135	g	
LINOLEIC ACID	450	mg	
VITAMINS:			
VITAMIN A	300	IU	
VITAMIN D	60	IU	
VITAMIN E	1.2	IU	
VITAMIN K	8.2	mcg	
THIAMINE (Vitamin B1)	60	mcg	
RIBOFLAVIN (Vitamin B2)	135	mcg	
VITAMIN B6	75	mcg	
VITAMIN B12	0.22	mcg	
NIACIN	750	mcg	
FOLIC ACID (Folacin)	9	mcg	
PANTOTHENIC ACID	450	mcg	
BIOTIN	2.2	mcg	

	Per 100 Calories	
VITAMIN C (Ascorbic Acid)	8	mg
CHOLINE	12	mg
INOSITOL	6.1	mg
MINERALS:		
CALCIUM	64	mg
PHOSPHORUS	36	mg
MAGNESIUM	6.7	mg
IRON	1.5	mg*
ZINC	0.75	mg
MANGANESE	7	mcg
COPPER	80	mcg
IODINE	8	mcg
SODIUM	24	mg
POTASSIUM	98	mg
CHLORIDE	59	mg
OTHERS:		
L-CARNITINE	10	mg/qt
TAURINE	50	mg/qt

*The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

REFERENCES:

1. Heiner D, Kim K: Allergy to foods. *American Journal of Asthma and Allergy for Pediatricians* 1988;1:32-38.
2. Kajosaari M: Food allergy in Finnish children aged 1 to 6 years. *Acta Paediatr Scand* 1982;71:815-819.
3. Bahna SL, Gandhi MD: Milk hypersensitivity: II. Practical aspects of diagnosis, treatment and prevention. *Ann Allergy* 1983;50:295.
4. Lothe L, Lindberg T, Jakobsson I: Cow's milk formula as a cause of infantile colic: A double-blind study. *Pediatrics* 1982;70:7-10.
5. Anglemeier AF, Montgomery MW: Amino acids, peptides and proteins, in Fennema OR (ed): *Principles of Food Science*. New York, Marcel Dekker Inc, 1976, p 248.
6. Data on file, Carnation Co, 1987.
7. Donovan GK, Torres-Pinedo R: Chronic diarrhea and soy formulas: Inhibition of diarrhea by lactose. *Am J Dis Child* 1987;141:1069-1071.
8. Groothius JR, Berman S, Chapman J: Effect of carbohydrate ingested on outcome in infants with mild gastroenteritis. *J Pediatr* 1986;108:903-906.
9. Committee on Nutrition, American Academy of Pediatrics: *Pediatric Nutrition Handbook*, ed 2, Forbes GB, Woodruff CW (eds). Elk Grove Village, Ill, American Academy of Pediatrics, 1985, p 278.
10. Vandenplas Y, Deneyer M, Sacre L, et al: Preliminary data on a field study with a new hypoallergic formula. *Eur J Pediatr*, to be published.
11. Kjellman NIM, Johansson SGO: Soy versus cow's milk in infants with a biparental history of atopic disease: Development of atopic disease and immunoglobulins from birth to 4 years of age. *Clin Allergy* 1979;9:347-358.
12. Schmidt E, Reinhardt D, Gerke R: The use of hypoallergenic milk formulas in newborns. *Der Kinderarzt* 1987;5:627-631.
13. Kahn A, Rebuffat E, Blum D, et al: Difficulty in initiating and maintaining sleep associated with cow's milk allergy in infants. *Sleep* 1987;10:116-121.
14. Zabransky S, Zabransky M: Preliminary clinical experience with hypoallergenic infant formula. *Extracta Paediatrica* 1987;11:10-12.
15. Passian K: Feeding newborns with Beba H.A. Data on file, Carnation Co, 1987.

NP-003 8/88

Summary

GOOD START H.A., the nutritionally complete, hypoallergenic infant formula with 100% whey protein:

- resolves symptoms of formula intolerance
- may prevent allergy symptoms in infants at high risk due to family history
- each batch is tested by two different methods to verify hypoallergenicity
- thoroughly researched in clinical trials and safely fed to more than 25,000 infants over the past 3 years in Europe
- is easily digestible—no curd formation in the stomach and a gastric emptying rate similar to that of breast milk
- has a vegetable fat blend with fat content similar to that of breast milk
- combines lactose and maltodextrin carbohydrates for enhanced absorption of calcium, magnesium, and zinc; appropriate osmolarity for optimal tolerance
- has pleasant taste, appearance, and aroma that may enhance parental compliance
- contains only low-molecular-weight hypoallergenic peptides; soy formulas contain potentially allergenic proteins
- in susceptible infants, symptoms of allergy occur far less frequently than the published incidences of symptoms with soy-based formulas

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(Please detach page, fold at both indicated lines, staple and mail.)

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(Please check boxes for desired items.)

☐ Please send me the GOOD START H.A.™ Product Monograph.

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NP-003 8/88

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Mycolog®-II

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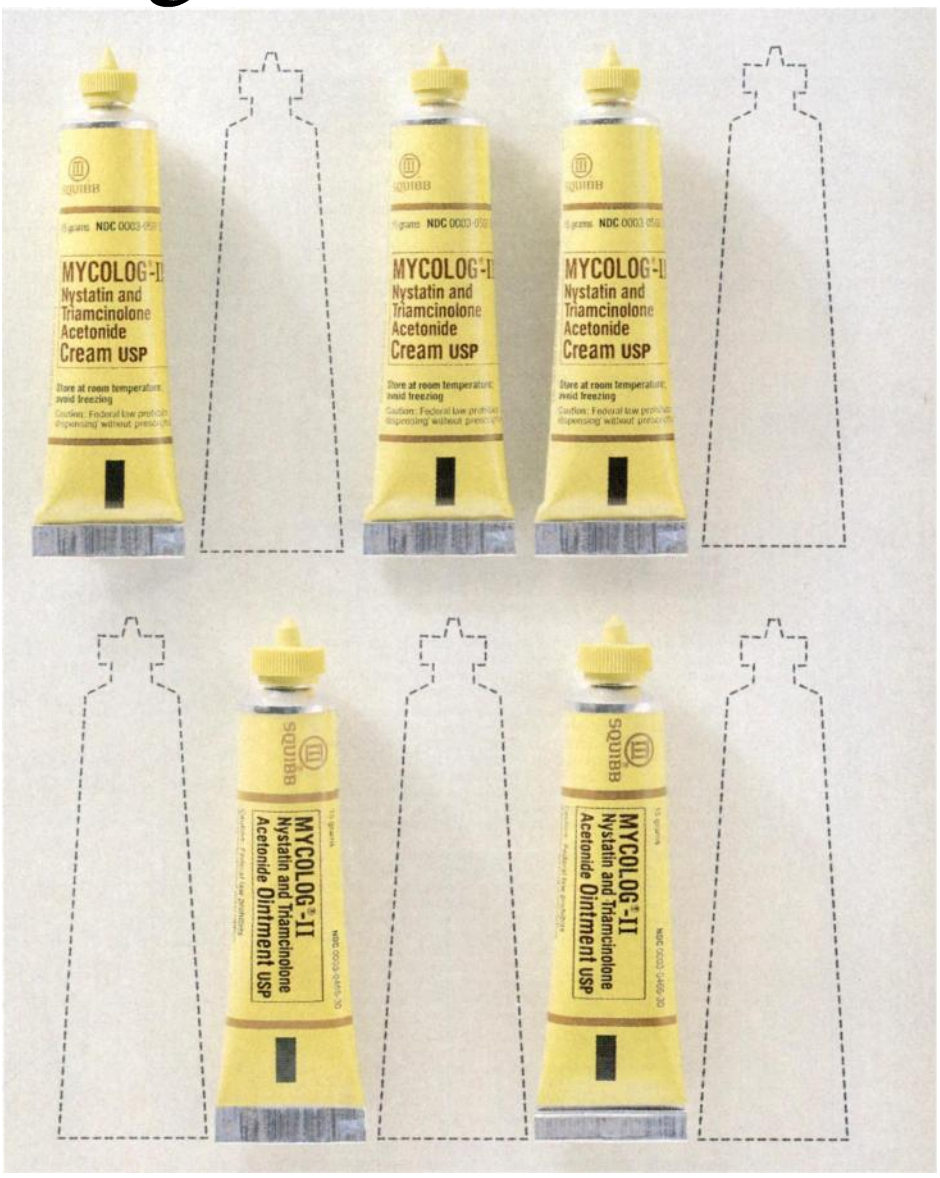
5 of your last 10 prescriptions did a disappearing act.



If you forgot to specify Mycolog®-II (Nystatin and Triamcinolone Acetonide Cream and Ointment), half of your patients received a generic substitute.*

Even if you prefer Mycolog-II because you know it works for your patients.

Even if you've come to rely on the Mycolog-II formula for antifungal, anti-inflammatory, antipruritic and vasoconstrictive activity.

Even if you prefer being sure with Squibb's quality control, the odds are fifty/fifty your patients won't see your prescription. Unless you specify "Do Not Substitute."

Remember to write D.A.W.†

*Data on file at Squibb

† Dispense As Written

SQUIBB®

See adjacent column for brief summary.

318-501

Issued: August 1988

MYCOLOG®-II
Nystatin and Triamcinolone Acetonide Cream and Ointment
For Dermatologic Use Only
Not for Ophthalmic Use

DESCRIPTION: MYCOLOG-II Cream and Ointment (Nystatin and Triamcinolone Acetonide Cream and Ointment) for dermatologic use provide 100,000 units of the antifungal agent nystatin and 1.0 mg of the synthetic corticosteroid triamcinolone acetonide per gram.

CONTRAINDICATIONS: This preparation is contraindicated in those patients with a history of hypersensitivity to any of its components.

PRECAUTIONS: General—Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions that augment systemic absorption include application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of any potent topical steroid applied to a large surface area should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests, and for impairment of thermal homeostasis. If HPA axis suppression or elevation of the body temperature occurs, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function and thermal homeostasis are generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (see PRECAUTIONS, Pediatric Use).

If irritation or hypersensitivity develops with the combination nystatin and triamcinolone acetonide, treatment should be discontinued and appropriate therapy instituted.

Laboratory Tests—If there is a lack of therapeutic response, appropriate microbiological studies (e.g., KOH smears and/or cultures) should be repeated to confirm the diagnosis and rule out other pathogens, before instituting another course of therapy.

A urinary free cortisol test and ACTH stimulation test may be helpful in evaluating hypothalamic-pituitary-adrenal (HPA) axis suppression due to corticosteroid.

Carcinogenesis, Mutagenesis, and Impairment of Fertility—Long-term animal studies have not been performed to evaluate carcinogenic or mutagenic potential, or possible impairment of fertility in males or females.

Pregnancy Category C—There are no teratogenic studies with combined nystatin and triamcinolone acetonide. Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. Therefore, any topical corticosteroid preparation should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Topical preparations containing corticosteroids should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers—It is not known whether any component of this preparation is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised during use of this preparation by a nursing woman.

Pediatric Use—In clinical studies of a limited number of pediatric patients ranging in age from two months through 12 years, nystatin-triamcinolone cream formulation cleared or significantly ameliorated the disease state in most patients.

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced hypothalamic-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS: A single case (approximately one percent of patients studied) of acneform eruption occurred with use of combined nystatin and triamcinolone acetonide in clinical studies.

Nystatin is virtually nontoxic and nonsensitizing and is well tolerated by all age groups, even during prolonged use. Rarely, irritation may occur.

The following local adverse reactions are reported infrequently with topical corticosteroids (reactions are listed in an approximate decreasing order of occurrence): burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria.

OVERDOSAGE: Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS, General); however, acute overdosage and serious adverse effects with dermatologic use are unlikely.

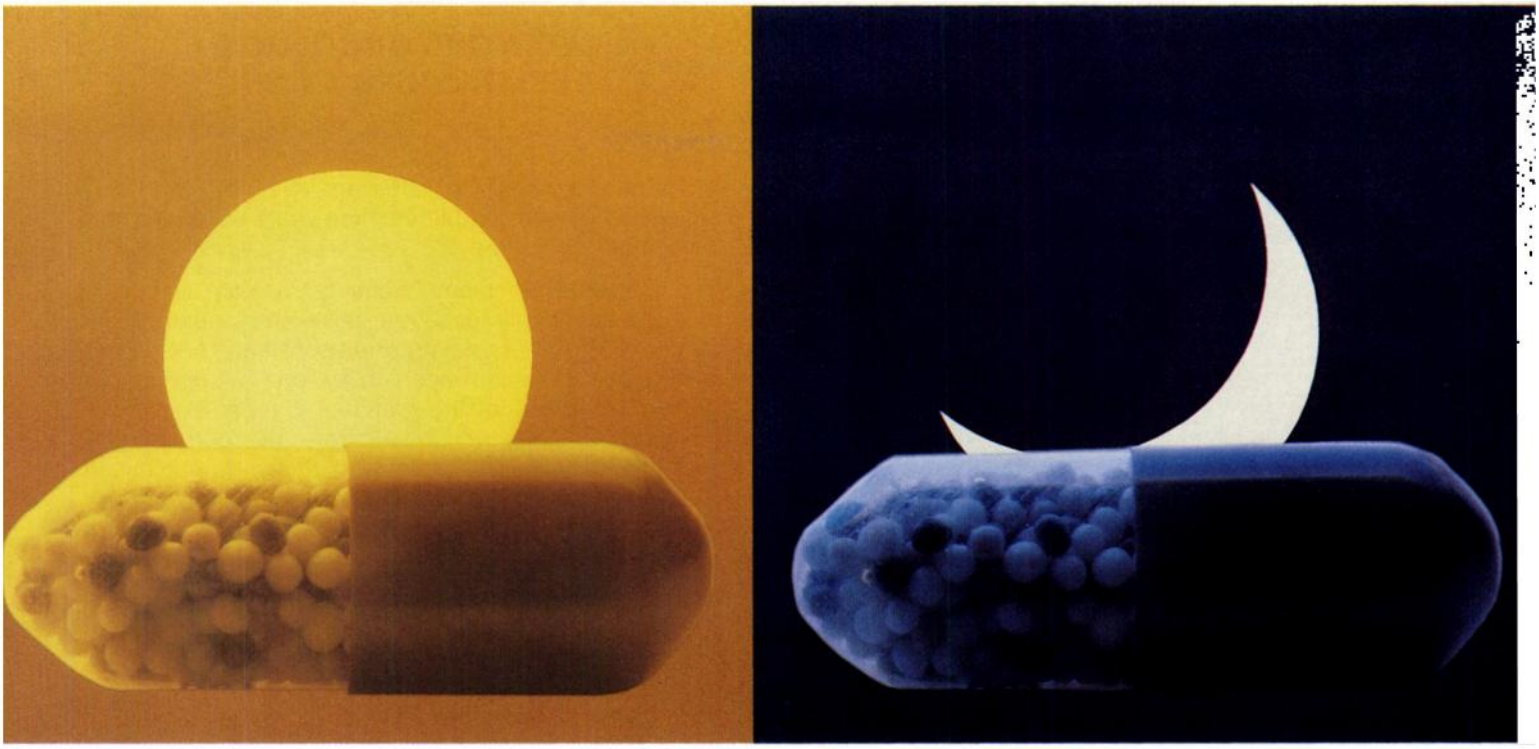
DOSAGE AND ADMINISTRATION: The use of these preparations should be discontinued if symptoms persist after 25 days of therapy (see PRECAUTIONS, Laboratory Tests). MYCOLOG-II Cream and Ointment should *not* be used with occlusive dressings.

HOW SUPPLIED: MYCOLOG-II Cream (Nystatin and Triamcinolone Acetonide Cream) is supplied in 15 g, 30 g, and 60 g tubes and 120 g jars.

MYCOLOG-II Ointment (Nystatin and Triamcinolone Acetonide Ointment) is supplied in 15 g, 30 g, and 60 g tubes and 120 g jars.

Storage—Store at room temperature; avoid freezing cream.

(J4-019/J4-024)



Pruritus relief– All day, All night.

Sustained release for sustained pruritus relief with

Temaril®
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Spansule® (sustained release capsules) **5 mg**

Temaril is the only antipruritic available in a 12-hour, sustained release capsule. Children over six years old can get the benefit of once-a-day dosing with this 5 mg Spansule.

And for children from six months to six years old, Temaril also comes in a pleasant-tasting, raspberry-flavored 2.5 mg/5 mL syrup and easy-to-swallow 2.5 mg tablets.

For over 30 years, Temaril has proven effective in relieving the pruritic symptoms associated with a wide range of conditions.

With Temaril, your pruritus patients will wake up smiling, not scratching.

Please see the following page for brief summary of prescribing information.

Herbert Laboratories
A SMITHKLINE BECKMAN COMPANY
Santa Ana, CA 92705

Temaril®

(trimeprazine tartrate)

INDICATIONS Treatment of pruritic symptoms in urticaria. Relief of pruritic symptoms in a variety of allergic and non-allergic conditions including atopic dermatitis, neurodermatitis, contact dermatitis, pityriasis rosea, poison ivy dermatitis, eczematous dermatitis, pruritus ani and vulvae, and drug rash.

CONTRAINDICATIONS Temaril (trimeprazine tartrate) is contraindicated: in comatose patients; in patients who have received large amounts of central nervous system depressants (alcohol, barbituates, narcotics, etc.); in patients with bone marrow depression; in patients who have demonstrated an idiosyncrasy or hypersensitivity to 'Temaril' or other phenothiazines; in newborn or premature children; and in nursing mothers. It should not be used in children who are acutely ill and/or dehydrated, as there is an increased susceptibility to dystonias in such patients.

WARNINGS Temaril (trimeprazine tartrate) may impair the mental and/or physical ability required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery. Similarly, it may impair mental alertness in children. The concomitant use of alcohol or other central nervous system depressants may have an additive effect. Patients should be warned accordingly.

'Temaril' should be used with extreme caution in patients with:

- Asthmatic attack
- Narrow-agle glaucoma
- Prostatic hypertrophy
- Stenosing peptic ulcer
- Pyloroduodenal obstruction
- Bladder neck obstruction
- Patients receiving monoamine oxidase inhibitors

Usage in Pregnancy: The safe use of 'Temaril' has not been established with respect to the possible adverse effects upon fetal development. Therefore, it should not be used in women of childbearing potential. Jaundice and prolonged extrapyramidal symptoms have been reported in infants whose mothers received phenothiazines during pregnancy.

Usage in Children: 'Temaril' should be used with caution in children who have a history of sleep apnea or a family history of sudden infant death syndrome (SIDS). It should also be used with caution in young children, in whom it may cause excitation.

Overdosage may produce hallucinations, convulsions and sudden death.

Usage in Elderly Patients (60 years or older): Elderly patients are more prone to develop the following side effects from phenothiazines:

- Hypotension
- Syncope
- Toxic confusional states
- Extrapyramidal symptoms, especially parkinsonism
- Excessive sedation

PRECAUTIONS Temaril (trimeprazine tartrate) may significantly affect the actions of other drugs. It may increase, prolong or intensify the sedative action of central nervous system depressants such as anesthetics, barbiturates or alcohol. When 'Temaril' is administered concomitantly the dose of a narcotic or barbiturate should be reduced to 1/4 or 1/2 the usual amount. In the patient with pain, receiving treatment with narcotics, excessive amounts of 'Temaril' may lead to restlessness and motor hyperactivity. 'Temaril' can block and even reverse the usual pressor effect of epinephrine.

'Temaril' should be used cautiously in persons with acute or chronic respiratory impairment, particularly children, as it may suppress the cough reflex.

This drug should be used cautiously in persons with cardiovascular disease, impairment of liver function, or those with a history of ulcer disease.

Since 'Temaril' has a slight antiemetic action, it may obscure signs of intestinal obstruction, brain tumor, or overdosage of toxic drugs.

Phenothiazines have been shown to elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent in vitro, a factor of potential importance if the prescribing of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

Drugs which lower the seizure threshold, including phenothiazine derivatives, should not be used with 'Amipaque'.* As with other phenothiazine derivatives, 'Temaril' should be discontinued at least 48 hours before myelography, should not be resumed for at least 24 hours postprocedure, and should not be used for the control of nausea and vomiting occurring either prior to myelography or postprocedure.

ADVERSE REACTIONS Temaril (trimeprazine tartrate) may produce adverse reactions attributable to both phenothiazines and antihistamines.

Note: Not all of the following adverse reactions have been reported with Temaril (trimeprazine tartrate); however, pharmacological similarities among the phenothiazine derivatives require that each be considered when 'Temaril' is administered. There have been occasional reports of sudden death in patients receiving phenothiazine derivatives chronically.

C.N.S. Effects: Drowsiness is the most common C.N.S. effect of this drug. Extrapyramidal reactions (opisthotonos, dystonia, akathisia, dyskinesia, parkinsonism) occur, particularly with high doses. (See Overdosage section for management of extrapyramidal symptoms). Hyperreflexia has been reported in the newborn when a phenothiazine was used during pregnancy. Other reported reactions include dizziness, headache, lassitude, tinnitus, incoordination, fatigue, blurred vision, euphoria, diplopia, nervousness, insomnia, tremors and grand mal seizures, excitation, catatonic-like states, neuritis and hysteria, oculogyric crises, disturbing dreams/nightmares, pseudoschizophrenia, and intensification and prolongation of C.N.S. depressants (opiates, analgesics, antihistamines, barbiturates, alcohol), atropine, heat, organophosphorus insecticides.

Cardiovascular Effects: Postural hypotension is the most common cardiovascular effect of phenothiazines. Reflex tachycardia may be seen. Bradycardia, faintness, dizziness and cardiac arrest have been reported. ECG changes, including blunting of T waves and prolongation of the Q-T interval, may be seen.

Gastrointestinal: Anorexia, nausea, vomiting, epigastric distress, diarrhea, constipation, and dry mouth may occur. Increased appetite and weight gain have also been reported.

Genitourinary: Urinary frequency and dysuria, urinary retention, early menses, induced lactation, gynecomastia, decreased libido, inhibition of ejaculation and false positive pregnancy tests have been reported.

Respiratory: Thickening of bronchial secretions, tightness of the chest, wheezing and nasal stuffiness may occur.

Allergic Reactions: These include urticaria, dermatitis, asthma, laryngeal edema, angioneurotic edema, photosensitivity, lupus erythematosus-like syndrome and anaphylactoid reactions.

Other Reported Reaction: Leukopenia, agranulocytosis, pancytopenia, hemolytic anemia, elevation of plasma cholesterol levels and thrombocytopenic purpura have been reported. Jaundice of the obstructive type has also been reported; it is usually reversible but chronic jaundice has been reported. Erythema, peripheral edema, and stomatitis have been reported. High or prolonged glucose tolerance curves, glycosuria, elevated spinal fluid proteins and reversed epinephrine effects may also occur.

Rare occurrences of neuroleptic malignant syndrome (NMS) have been reported in patients receiving phenothiazines. This syndrome is comprised of the symptom complex of hyperthermia, altered consciousness, muscular rigidity and autonomic dysfunction and is potentially fatal.

Long-Term Therapy Considerations: After prolonged phenothiazine administration at high dosage, pigmentation of the skin has occurred, chiefly in the exposed areas. Ocular changes consist of the appearance of lenticular and corneal opacities, epithelial keratopathies and pigmentary retinopathy. Vision may be impaired.

*Trademark Reg. U.S. Pat. Off.: 'Amipaque' for metrizamide, distributed by Winthrop-Breon Laboratories.

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PEDIATRIC ONCOLOGY FELLOWSHIPS AT NIH

The National Cancer Institute, National Institutes of Health, is accepting applications for fellowships in pediatric oncology. Positions are available to physicians who have completed three years of training in pediatrics.

The Pediatric Oncology Training Program is considering applicants for 3-year fellowships beginning July 1, 1990. This 3-year program consists of one year of primary clinical responsibility on the pediatric oncology service of the National Cancer Institute. Rotations in pediatric hematology are coordinated with the NIH Clinical Center and affiliated hospitals. The second and third years consist of an individualized program of laboratory research and clinical investigations.

Emphasis is placed on continuity of patient care, principles of patient management, and design and conduct of clinical trials. Seminars, lectures, and conferences deal with a variety of related subjects including biostatistics, immunology, epidemiology, cell biology, cell kinetics, molecular biology, virology, genetics, clinical pharmacology, diagnostic pathology, and radiobiology.

The laboratory aspects of the program are directed at training Fellows to become independent investigators. Topics under investigation in the Pediatric Branch include the cellular and molecular biology of pediatric tumors, clinical pharmacology, immunology, and the study of host defenses against infection. Fellows may also seek laboratory opportunities throughout the Division of Cancer Treatment. In addition, there are ample opportunities for participation in clinical research topics.

Medical Staff Fellows will be assigned to Civil Service positions with an annual salary of $32,000 and an increase of $2,000 for each additional year up to a maximum of $36,000. Medical Staff Fellows will receive all benefits including health insurance, life insurance options, vacation and sick leave. In addition, moving, travel expenses for the Fellow and Federal health care benefits are available. For further information please contact:

Philip A. Pizzo, M.D.
Chief, Pediatric Branch
National Cancer Institute
National Institutes of Health
Building 10, Room 13N240
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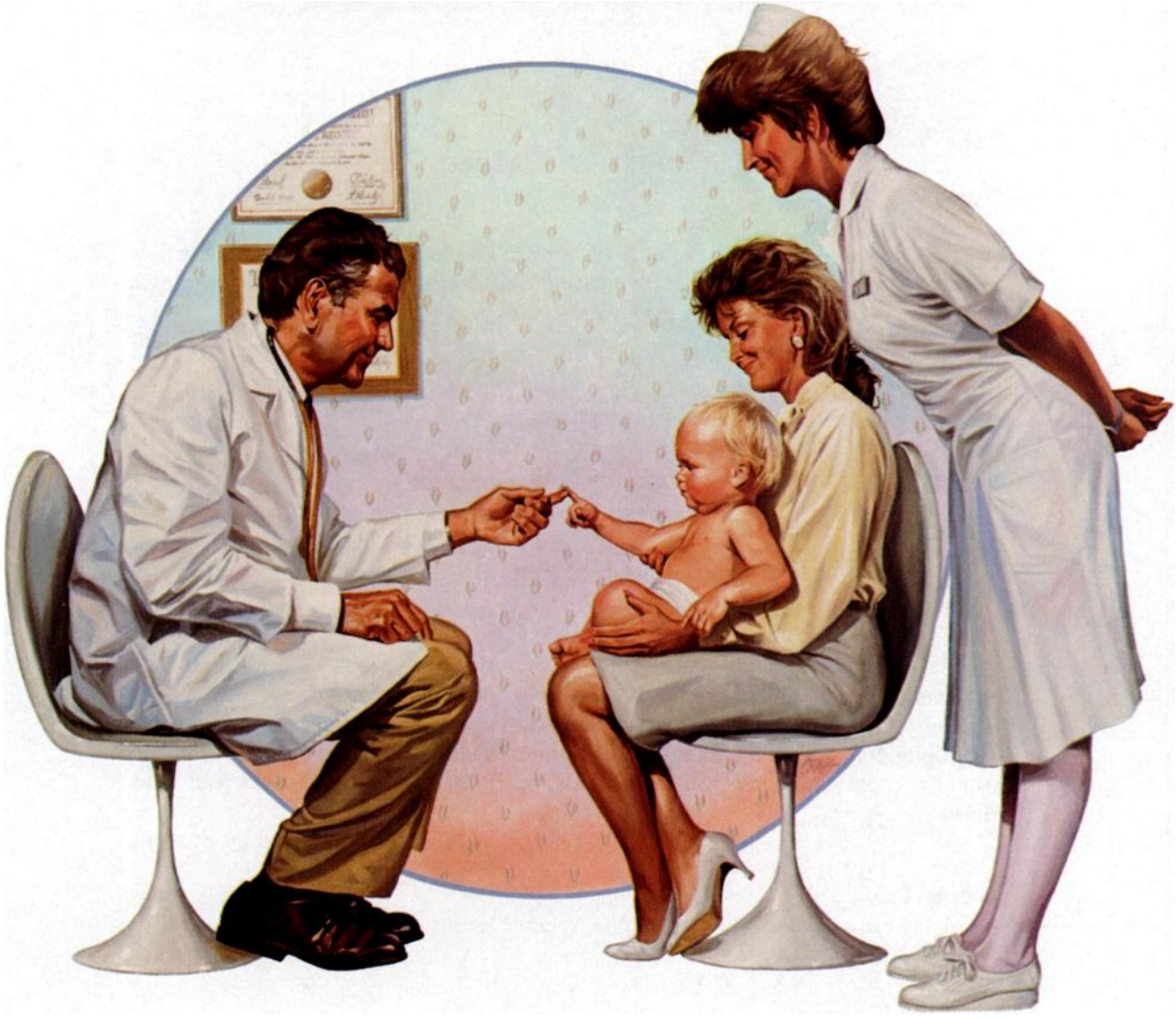

LIQUIPRIN has earned the confidence of parents and pediatricians with dependable relief of fever and pain for over 25 years.

The LIQUIPRIN acetaminophen formula does not contain aspirin or alcohol and has a pleasant-tasting fruit flavor that babies like.

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NORTHERN MODEL

The Nordic countries have long been an example for good health care; a new study* sets out in detail the evidence that children are healthier in Scandinavia than almost anywhere else in the world.

Submitted by Student

* Kohler L, Jacobsson G: *Children's health and well-being in the Nordic Countries.* Clinical Developments in Medicine, No. 98. Oxford, England, Mackeith Press, 1987.
Quoted in *Lancet*, April 9, 1988.

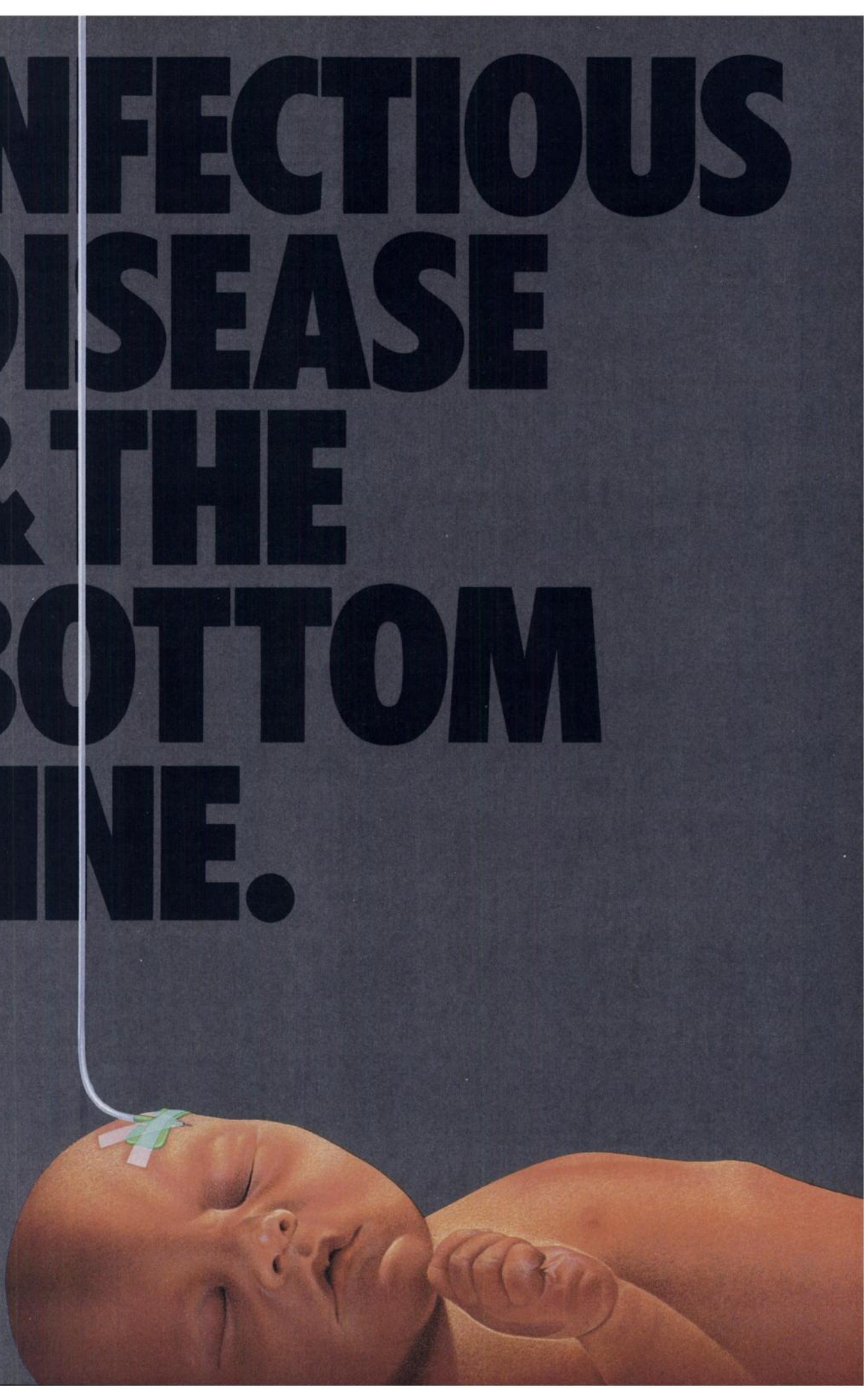
SQUEAKY WHEEL GOT THE GREASE

The millions of dollars for Tylenol investigations [in 1982] yielded little beyond the probability that some lone crackpot had tampered with a few boxes of the pain reliever.... By comparison 634 Americans had been stricken with AIDS by October 5, 1982. Of these, 260 were dead. There was no rush to spend money, mobilize public health officials, or issue regulations that would save lives.

Submitted by Student

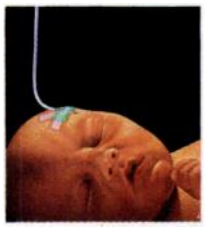
From Shilts R: *And the Band Played On.* New York, St. Martin's Press, 1987.

INFECTIOUS DISEASE & THE BOTTOM LINE.




q8h/q12h

The right antibiotic at the right time. The bottom line in infectious disease.



For six years, Claforan® has been the right antibiotic for countless patients—with q8h dosing for moderate-to-severe infections, and q12h dosing for uncomplicated infections. From meningitis in neonates to pneumonia in the elderly, it has established an outstanding record of success. And, Claforan® provides the flexibility of q6-8h dosing for severe infections, and q4h dosing for life-threatening infections.

The efficacy and safety of Claforan® are uncompromised. In neonates it has the potential for less of an impact on fecal flora than ceftriaxone or cefoperazone.[1] That's why Claforan® is preferred by leading pediatric authorities.[2-4] In patients of all ages, it has not been shown to cause coagulation abnormalities, disulfiram-like reactions, nephrotoxicity, ototoxicity, or seizures.

Right for cost containment with q8h/q12h dosing. The bottom line in today's hospital environment.

Claforan® saves money as well, with economical q12h dosing in uncomplicated infections and q8h dosing in moderate-to-severe infections. In fact, data on over 2,000 cases show that Claforan® q8h for moderate-to-severe infections and q12h for uncomplicated infections consistently maintained a high level of efficacy.[5]

Clearly, what's best about cephalosporins is what you get with Claforan®

STERILE & INJECTION

Claforan®

(cefotaxime sodium)

Please see following page for references and brief summary of prescribing information.

The bottom line.

References: 1. Guggenbichler JP, Kofler J, Allerberger F: The influence of third-generation cephalosporins on the aerobic intestinal flora. *Infection* 1985;13(Suppl 1):137-139. 2. Klein JO, Feigin RD, McCracken GH: Report of the task force on diagnosis and management of meningitis. *Pediatrics* 1986;78(5):959-982. 3. McCracken GH: New antimicrobial agents for pediatricians. *Pediatr Infect Dis* 1985;S10-S12. 4. Report of the Committee on Infectious Diseases. American Academy of Pediatrics. Elk Grove Village, Illinois, 1986; 150-170. 5. Parker RH: Effect of frequency of administration on therapeutic efficacy of cefotaxime. *Clin Ther* 1984;6:488-499.

Convenient, economical q8h/q12h dosing

STERILE & INJECTION

Claforan®

(cefotaxime sodium)*

Brief Summary

INDICATIONS AND USAGE

Treatment

Claforan is indicated for the treatment of patients with serious infections caused by susceptible strains of the designated microorganisms in the diseases listed below.

(1) **Lower respiratory tract infections,** including pneumonia, caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*), *Streptococcus pyogenes*† (Group A streptococci) and other streptococci (excluding enterococci, e.g., *Streptococcus faecalis*), *Staphylococcus aureus* (penicillinase and non-penicillinase producing), *Escherichia coli*, *Klebsiella* species, *Haemophilus influenzae* (including ampicillin-resistant strains), *Haemophilus parainfluenzae*, *Proteus mirabilis*, *Serratia marcescens*†, *Enterobacter* species, indole-positive *Proteus* and *Pseudomonas* species (including *P. aeruginosa*).

(2) **Genitourinary infections.** Urinary tract infections caused by *Enterococcus* species, *Staphylococcus epidermidis*, *Staphylococcus aureus*† (penicillinase and non-penicillinase producing), *Citrobacter* species, *Enterobacter* species, *Escherichia coli*, *Klebsiella* species, *Proteus mirabilis*, *Proteus vulgaris*†, *Proteus inconstans* Group B, *Morganella morganii*†, *Providencia rettgeri*†, *Serratia marcescens*, and *Pseudomonas* species (including *P. aeruginosa*). Also, uncomplicated gonorrhea of single or multiple sites caused by *Neisseria gonorrhoeae*, including penicillinase producing strains.

(3) **Gynecologic infections,** including pelvic inflammatory disease, endometritis and pelvic cellulitis caused by *Staphylococcus epidermidis*, *Streptococcus* species, *Enterococcus* species, *Enterobacter* species†, *Klebsiella* species†, *Escherichia coli*, *Proteus mirabilis*, *Bacteroides* species (including *Bacteroides fragilis*†), *Clostridium* species, anaerobic cocci (including *Peptostreptococcus* species and *Peptococcus* species) and *Fusobacterium* species (including *F. nucleatum*†).

(4) **Bacteremia/Septicemia** caused by *Escherichia coli*, *Klebsiella* species, *Serratia marcescens*, *Staphylococcus aureus*, and *Streptococcus* species (including *S. pneumoniae*).

(5) **Skin and skin structure infections** caused by *Staphylococcus aureus* (penicillinase and non-penicillinase producing), *Staphylococcus epidermidis*, *Streptococcus pyogenes* (Group A streptococci) and other streptococci, *Enterococcus* species, *Acinetobacter* species†, *Escherichia coli*, *Citrobacter* species (including *C. freundii*†), *Enterobacter* species, *Klebsiella* species, *Proteus mirabilis*, *Proteus vulgaris*†, *Morganella morganii*, *Providencia rettgeri*†, *Pseudomonas* species, *Serratia marcescens*, *Bacteroides* species, and anaerobic cocci (including *Peptostreptococcus*† species and *Peptococcus* species).

(6) **Intra-abdominal infections** including peritonitis caused by *Streptococcus* species†, *Escherichia coli*, *Klebsiella* species, *Bacteroides* species, anaerobic cocci (including *Peptostreptococcus*† species and *Peptococcus*† species), *Proteus mirabilis*†, and *Clostridium* species†.

(7) **Bone and/or joint infections** caused by *Staphylococcus aureus* (penicillinase and non-penicillinase producing strains), *Streptococcus* species (including *S. pyogenes*†), *Pseudomonas* species (including *P. aeruginosa*†), and *Proteus mirabilis*†.

(8) **Central nervous system infections,** e.g., meningitis and ventriculitis, caused by *Neisseria meningitidis*, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*†, and *Escherichia coli*†.

† Efficacy for this organism, in this organ system, has been studied in fewer than 10 infections.

Although many strains of enterococci (e.g., *S. faecalis*) and *Pseudomonas* species are resistant to cefotaxime sodium *in vitro*, Claforan has been used successfully in treating patients with infections caused by susceptible organisms.

Specimens for bacteriologic cultures should be obtained prior to therapy in order to isolate and identify causative organisms and to determine their susceptibilities to Claforan. Therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly.

Prevention

The administration of Claforan preoperatively reduces the incidence of certain infections in patients undergoing surgical procedures (e.g., abdominal or vaginal hysterectomy, gastrointestinal and genitourinary tract surgery) that may be classified as contaminated or potentially contaminated.

In patients undergoing cesarean section, intraoperative (after clamping the umbilical cord) and postoperative use of Claforan may also reduce the incidence of certain postoperative infections. (See **DOSAGE AND ADMINISTRATION** section.)

Effective use for elective surgery depends on the time of administration. To achieve effective tissue levels, Claforan should be given ½ to 1½ hours before surgery. (See **DOSAGE AND ADMINISTRATION** section.)

For patients undergoing gastrointestinal surgery, preoperative bowel preparation by mechanical cleansing as well as with a non-absorbable antibiotic (e.g., neomycin) is recommended.

If there are signs of infection, specimens for culture should be obtained for identification of the causative organism so that appropriate therapy may be instituted.

CONTRAINDICATIONS

Claforan is contraindicated in patients who have shown hypersensitivity to cefotaxime sodium or the cephalosporin group of antibiotics.

WARNINGS

BEFORE THERAPY WITH CLAFORAN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFOTAXIME SODIUM, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN WITH CAUTION TO PATIENTS WITH TYPE I HYPERSENSITIVITY REACTIONS TO PENICILLIN. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO CLAFORAN OCCURS, DISCONTINUE TREATMENT WITH THE DRUG. SERIOUS HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*.

Mild cases of colitis may respond to drug discontinuance alone.

Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should also be considered.

PRECAUTIONS

Claforan® (cefotaxime sodium) should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Claforan has not been shown to be nephrotoxic; however, because high and prolonged serum antibiotic concentrations can occur from usual doses in patients with transient or persistent reduction of urinary output because of renal insufficiency, the total daily dosage should be reduced when Claforan is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organism.

Although there is no clinical evidence supporting the necessity of changing the dosage of cefotaxime sodium in patients with even profound renal dysfunction, it is suggested that, until further data are obtained, the dose of cefotaxime sodium be halved in patients with estimated creatinine clearances of less than 20 mL/min/1.73 m².

When only serum creatinine is available, the following formula (based on sex, weight, and age of the patient) may be used to convert this value into creatinine clearance. The serum creatinine should represent a steady state of renal function.

$$\text{Males:}\ \frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine}}$$

$$\text{Females:}\ 0.85 \times \text{above value}$$

As with other antibiotics, prolonged use of Claforan may result in overgrowth of nonsusceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Drug Interactions: Increased nephrotoxicity has been reported following concomitant administration of cephalosporins and aminoglycoside antibiotics.

Carcinogenesis, Mutagenesis: Long-term studies in animals have not been performed to evaluate carcinogenic potential. Mutagenic tests included a micronucleus and an Ames test. Both tests were negative for mutagenic effects.

Pregnancy (Category B): Reproduction studies have been performed in mice and rats at doses up to 30 times the usual human dose and have revealed no evidence of impaired fertility or harm to the fetus because of cefotaxime sodium. However, there are no well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects: Use of the drug in women of childbearing potential requires that the anticipated benefit be weighed against the possible risks.

In perinatal and postnatal studies with rats, the pups in the group given 1200 mg/kg of Claforan were significantly lighter in weight at birth and remained smaller than pups in the control group during the 21 days of nursing.

Nursing Mothers: Claforan is excreted in human milk in low concentrations. Caution should be exercised when Claforan is administered to a nursing woman.

ADVERSE REACTIONS

Claforan is generally well tolerated. The most common adverse reactions have been local reactions following IM or IV injection. Other adverse reactions have been encountered infrequently.

The most frequent adverse reactions (greater than 1%) are:

Local (4.3%)—Injection site inflammation with IV administration. Pain, induration, and tenderness after IM injection.

Hypersensitivity (2.4%)—Rash, pruritus, fever, and eosinophilia.

Gastrointestinal (1.4%)—Colitis, diarrhea, nausea, and vomiting.

Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment.

Nausea and vomiting have been reported rarely.

Less frequent adverse reactions (less than 1%) are:

Hemic and Lymphatic System—Granulocytopenia, transient leukopenia, eosinophilia, neutropenia, and thrombocytopenia have been reported. Some individuals have developed positive direct Coombs Tests during treatment with the cephalosporin antibiotics.

Genitourinary System—Moniliasis, vaginitis.

Central Nervous System—Headache.

Liver—Transient elevations in SGOT, SGPT, serum LDH, and serum alkaline phosphatase levels have been reported.

Kidney—As with some other cephalosporins, transient elevations of BUN have been occasionally observed with Claforan.

DOSAGE AND ADMINISTRATION

Adults

Dosage and route of administration should be determined by susceptibility of the causative organisms, severity of the infection, and the condition of the patient (see table for dosage guidelines). Claforan may be administered IM or IV after reconstitution. Premixed Claforan Injection is intended for IV administration after thawing. The maximum daily dosage should not exceed 12 grams.

GUIDELINES FOR DOSAGE OF CLAFORAN

Type of Infection	Daily Dose (grams)	Frequency and Route
Gonorrhea	1	1 gram IM (single dose)
Uncomplicated infections	2	1 gram every 12 hours IM or IV
Moderate to severe infections	3-6	1-2 grams every 8 hours IM or IV
Infections commonly needing antibiotics in higher dosage (e.g., septicemia)	6-8	2 grams every 6-8 hours IV
Life-threatening infections	up to 12	2 grams every 4 hours IV

To prevent postoperative infection in contaminated or potentially contaminated surgery, the recommended dose is a single 1 gram IM or IV administered 30 to 90 minutes prior to start of surgery.

Cesarean Section Patients

The first dose of 1 gram is administered intravenously as soon as the umbilical cord is clamped. The second and third doses should be given as 1 gram intravenously or intramuscularly at 6 and 12 hours after the first dose.

Neonates, Infants, and Children

The following dosage schedule is recommended:

Neonates (birth to 1 month):

0-1 week of age	50 mg/kg IV q12h
1-4 weeks of age	50 mg/kg IV q8h

It is not necessary to differentiate between premature and normal gestational age infants.

Infants and Children (1 month to 12 years): For body weights less than 50 kg, the recommended daily dose is 50 to 180 mg/kg IM or IV of body weight divided into four to six equal doses. The higher dosages should be used for more severe or serious infections, including meningitis. For body weights 50 kg or more, the usual adult dosage should be used; the maximum daily dosage should not exceed 12 grams.

Impaired Renal Function—see **PRECAUTIONS** section.

NOTE: As with antibiotic therapy in general, administration of Claforan should be continued for a minimum of 48 to 72 hours after the patient defervesces or after evidence of bacterial eradication has been obtained; a minimum of 10 days of treatment is recommended for infections caused by Group A beta-hemolytic streptococci in order to guard against the risk of rheumatic fever or glomerulonephritis; frequent bacteriologic and clinical appraisal is necessary during therapy of chronic urinary tract infection and may be required for several months after therapy has been completed; persistent infections may require treatment of several weeks and doses smaller than those indicated above should not be used.

*US Patent 4,152,432 CLAFORAN® REG TM ROUSSEL-UCLAF

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Q74283-988

Hoechst-Roussel Pharmaceuticals Inc.
Somerville, New Jersey 08876

Hoechst

Why send an antitussive to do a bronchodilator's job?

- ☐ Asthma is the most common cause of persistent episodic cough in children.[1,2]
- ☐ PROVENTIL Syrup has been proven to reduce nighttime cough symptoms due to asthma as much as 50%.[3]
- ☐ Starts within 30 minutes—lasts up to 6 hours.
- ☐ Safe enough for 2 year olds.
- ☐ Completely free of sugar, alcohol, tartrazine (yellow dye No. 5), and bisulfites.
- ☐ Pleasant tasting and easy to take.

References: 1. Cloutier MM: The coughing child: Etiology and treatment of a common symptom. *Postgrad Med* 1983;73:169-175. **2.** Miser WF: Variant forms of asthma. *Am Fam Physician* 1987;35(6):89-96. **3.** Rachelefsky GS, Katz RM, Siegel SC: Albuterol syrup in the treatment of the young asthmatic child. *Ann Allergy* 1981;47:143-146.

Proven

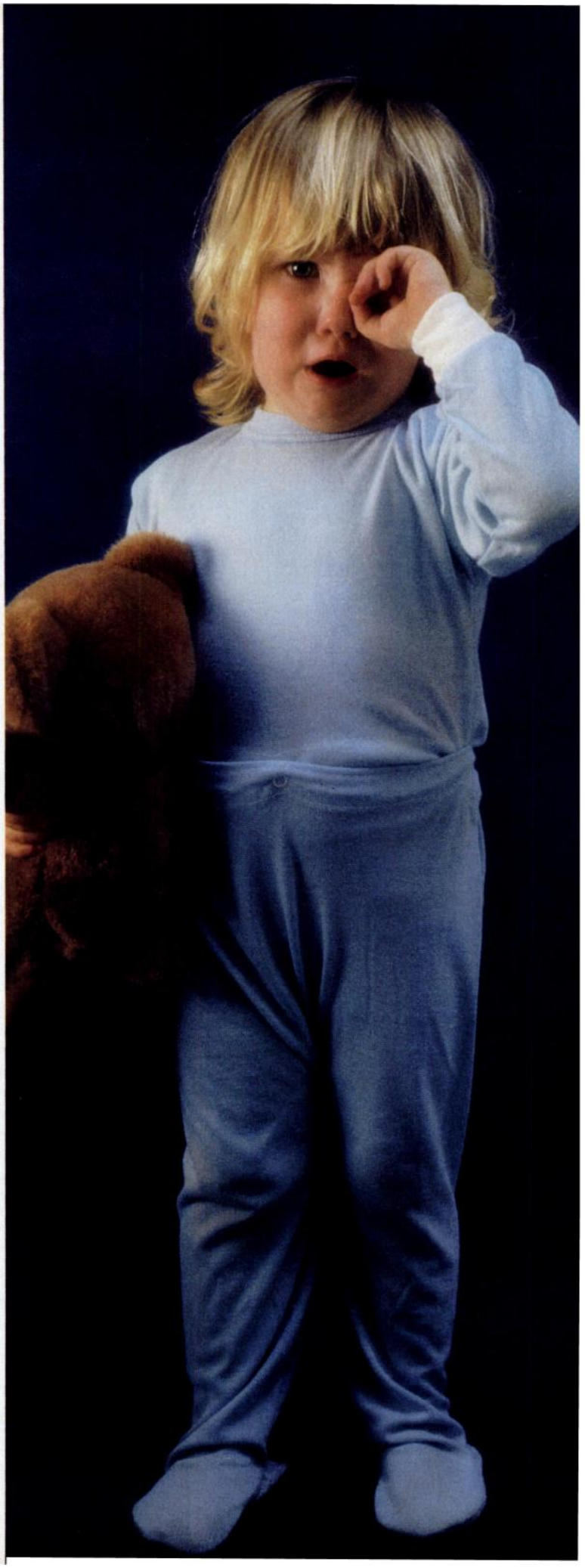
Proventil®

(albuterol sulfate) **Syrup**

2 mg albuterol per 5 ml

Stops coughs asthma starts.

Please see next page for brief summary of prescribing information.



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Proven
Proventil®
(albuterol sulfate) Syrup

2 mg albuterol per 5 ml

INDICATIONS AND USAGE PROVENTIL Syrup is indicated for the relief of bronchospasm in adults and in children 2 years of age and older with reversible obstructive airway disease.

In controlled clinical trials in patients with asthma, the onset of improvement in pulmonary function, as measured by maximal midexpiratory flow rate (MMEF) and forced expiratory volume in one second (FEV_1), was within 30 minutes after a dose of PROVENTIL Syrup. Peak improvement of pulmonary function occurred between 2 to 3 hours. In a controlled clinical trial involving 55 children, clinically significant improvement (defined as maintenance of mean values over baseline of 15% or 20% or more in the FEV_1 and MMEF respectively) continued to be recorded up to 6 hours. No decrease in the effectiveness was reported in one uncontrolled study of 32 children who took PROVENTIL Syrup for a 3-month period.

CONTRAINDICATIONS PROVENTIL Syrup is contraindicated in patients with a history of hypersensitivity to any of its components.

PRECAUTIONS General: Although albuterol usually has minimal effects on the beta$_1$-adrenoceptors of the cardiovascular system at the recommended dosage, occasionally the usual cardiovascular and CNS stimulatory effects common to all sympathomimetic agents have been seen with patients treated with albuterol necessitating discontinuation. Therefore, albuterol should be used with caution in patients with cardiovascular disorders, including coronary insufficiency and hypertension, in patients with hyperthyroidism or diabetes mellitus, and in patients who are unusually responsive to sympathomimetic amines.

Large doses of intravenous albuterol have been reported to aggravate preexisting diabetes mellitus and ketoacidosis. Additionally, albuterol and other beta-agonists, when given intravenously, may cause a decrease in serum potassium, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation. The relevance of these observations to the use of PROVENTIL Syrup is unknown.

Information for Patients: The action of PROVENTIL Syrup may last up to six hours and therefore it should not be taken more frequently than recommended. Do not increase the dose or frequency of medication without medical consultation. If symptoms get worse, medical consultation should be sought promptly.

Drug Interactions: The concomitant use of PROVENTIL Syrup and other oral sympathomimetic agents is not recommended since such combined use may lead to deleterious cardiovascular effects. This recommendation does not preclude the judicious use of an aerosol bronchodilator of the adrenergic stimulant type in patients receiving PROVENTIL Syrup. Such concomitant use, however, should be individualized and not given on a routine basis. If regular coadministration is required, then alternative therapy should be considered.

Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of albuterol on the vascular system may be potentiated.

Beta-receptor blocking agents and albuterol inhibit the effect of each other.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Albuterol sulfate, like other agents in its class, caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium in a 2-year study in the rat, at doses corresponding to 2, 9, and 46 times the maximum human (child weighing 21 kg) oral dose. In another study this effect was blocked by the coadministration of propranolol. The relevance of these findings to humans is not known. An 18-month study in mice and a lifetime study in hamsters revealed no evidence of tumorigenicity. Studies with albuterol revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Teratogenic Effects—Pregnancy Category C: Albuterol has been shown to be teratogenic in mice when given subcutaneously in doses corresponding to 0.2 times the maximum human (child weighing 21 kg) oral dose. There are no adequate and well-controlled studies in pregnant women. Albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A reproduction study in CD-1 mice with albuterol showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg; none was observed at 0.025 mg/kg. Cleft palate also occurred in 22 of 72 (30.5%) fetuses treated with 2.5 mg/kg isoproterenol (positive control). A reproduction study in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) fetuses at 50 mg/kg, corresponding to 46 times the maximum human (child weighing 21 kg) oral dose of albuterol sulfate.

Labor and Delivery: Oral albuterol has been shown to delay preterm labor in some reports. There are presently no well-controlled studies which demonstrate that it will stop preterm labor or prevent labor at term. Therefore, cautious use of PROVENTIL Syrup is required in pregnant patients when given for relief of bronchospasm so as to avoid interference with uterine contractibility. Use in such patients should be restricted to those patients in whom the benefits clearly outweigh the risks.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children below the age of 2 years have not yet been adequately demonstrated.

ADVERSE REACTIONS The adverse reactions to albuterol are similar in nature to those of other sympathomimetic agents. The most frequent adverse reactions to PROVENTIL Syrup in adults and older children were tremor, 10 of 100 patients; nervousness and shakiness, each 9 of 100 patients. Other reported adverse reactions were headache, 4 of 100 patients; dizziness and increased appetite, each 3 of 100 patients; hyperactivity and excitement, each 2 of 100 patients; tachycardia, epistaxis, irritable behavior, and sleeplessness, each 1 of 100 patients. The following adverse effects occurred in less than 1 of 100 patients each: muscle spasm, disturbed sleep; epigastric pain; cough; palpitations; stomach ache; irritable behavior; dilated pupils; sweating; chest pain; weakness.

In young children 2 to 6 years of age, some adverse reactions were noted more frequently than in adults and older children. Excitement was noted in approximately 20% of patients and nervousness in 15%. Hyperkinesia occurred in 4% of patients; insomnia, tachycardia, and gastrointestinal symptoms in 2% each. Anorexia, emotional lability, pallor, fatigue, and conjunctivitis were seen in 1%.

In addition, albuterol, like other sympathomimetic agents, can cause adverse reactions such as hypertension, angina, vomiting, vertigo, central nervous system stimulation, unusual taste, and drying or irritation of the oropharynx.

The reactions are generally transient in nature, and it is usually not necessary to discontinue treatment with PROVENTIL Syrup. In selected cases, however, dosage may be reduced temporarily; after the reaction has subsided, dosage should be increased in small increments to the optimal dosage.

OVERDOSAGE Manifestations of overdosage include anginal pain, hypertension, hypokalemia, and exaggeration of the effects listed in **ADVERSE REACTIONS**.

The oral LD_{50} in rats and mice was greater than 2,000 mg/kg. Dialysis is not appropriate treatment for overdosage of PROVENTIL Syrup. The judicious use of a cardioselective beta-receptor blocker, such as metoprolol tartrate, is suggested, bearing in mind the danger of inducing an asthmatic attack.

For more complete details, consult package insert or Schering literature available from your Schering representative or Professional Services Department, Schering Corporation, Kenilworth, NJ 07033.

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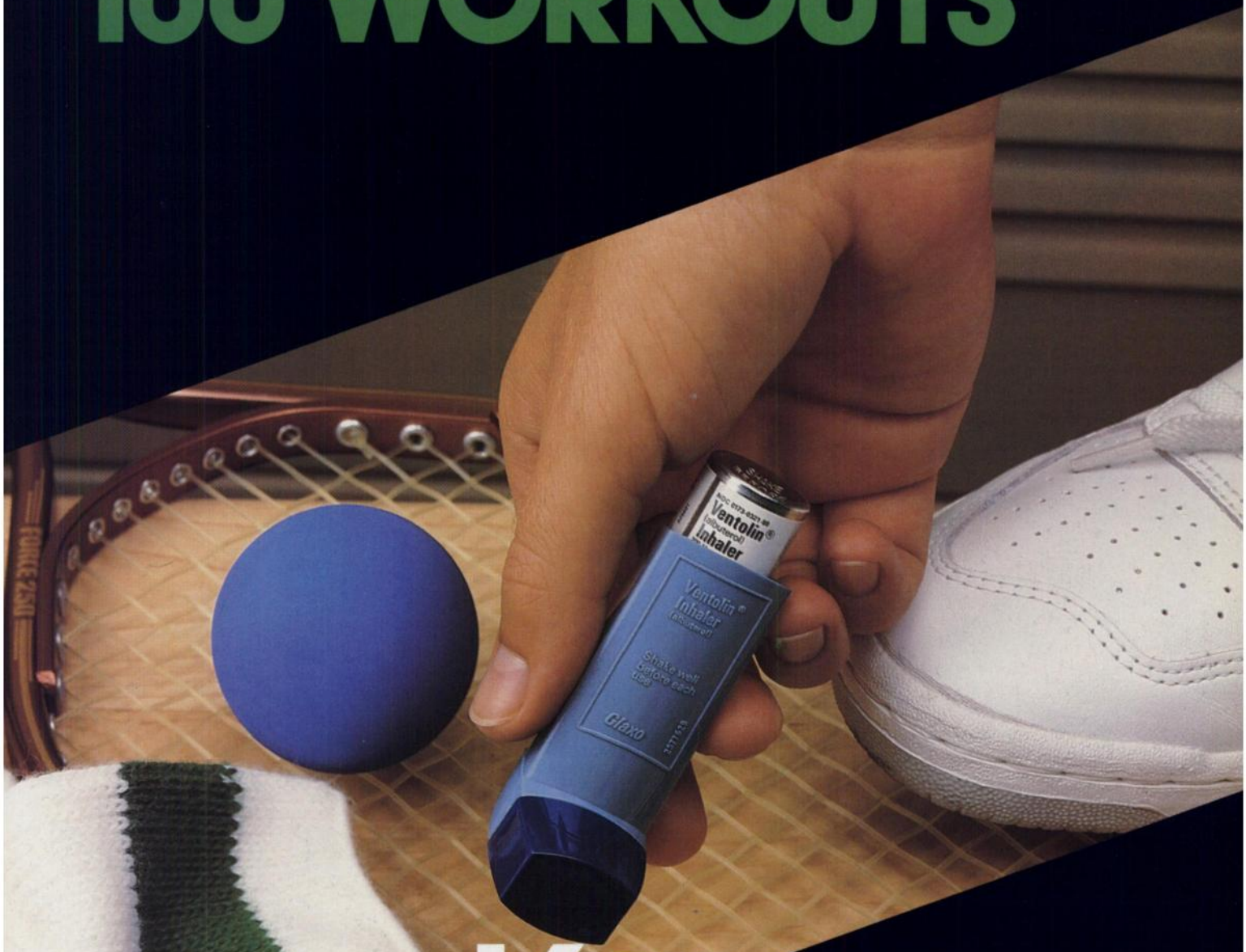

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(ALBUTEROL)
INHALER

First-line prophylaxis for exercise-induced bronchospasm (EIB)—
contains at least 100 two-puff doses to be taken 15 minutes before every workout. Works fast...protects for up to 6 hours in most patients.

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Please consult next page for Brief Summary of Prescribing Information

VENTOLIN® (ALBUTEROL) INHALER /AND REFILL

First-line prophylaxis for exercise-induced bronchospasm (EIB)... First-line therapy for bronchospasm

- Two inhalations 15 minutes before exercise protect against EIB for up to 6 hours in most patients
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- Proven long-term efficacy for the reversible bronchospastic component of obstructive airway disease
- Minimal cardiac stimulation at recommended doses*

*Sympathomimetic amines should be used with caution in patients with cardiovascular disorders.

VIN 315R • Printed in USA • October 1988

VENTOLIN® (albuterol) Inhaler **BRIEF SUMMARY**
Bronchodilator Aerosol
For Oral Inhalation Only

The following is a brief summary only. Before prescribing, see complete prescribing information in VENTOLIN® Inhaler product labeling.

CONTRAINDICATIONS: VENTOLIN® Inhaler is contraindicated in patients with a history of hypersensitivity to any of its components.

WARNINGS: As with other inhaled beta-adrenergic agonists, VENTOLIN® Inhaler can produce paradoxical bronchospasm that can be life-threatening. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted.

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. The exact cause of death is unknown, but cardiac arrest following the unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected.

Immediate hypersensitivity reactions may occur after administration of albuterol inhaler, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema.

The contents of VENTOLIN® Inhaler are under pressure. Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 120°F may cause bursting. Never throw container into fire or incinerator. Keep out of reach of children.

PRECAUTIONS: General: Albuterol, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias and hypertension; in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines.

Large doses of intravenous albuterol have been reported to aggravate pre-existing diabetes mellitus and ketoacidosis. Additionally, beta-agonists, including albuterol, given intravenously may cause a decrease in serum potassium, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation. The relevance of these observations to the use of VENTOLIN® Inhaler is unknown, since the aerosol dose is much lower than the doses given intravenously.

Although there have been no reports concerning the use of VENTOLIN Inhaler during labor and delivery, it has been reported that high doses of albuterol administered intravenously inhibit uterine contractions. Although this effect is extremely unlikely as a consequence of aerosol use, it should be kept in mind.

Information For Patients: The action of VENTOLIN Inhaler may last up to six hours, and therefore it should not be used more frequently than recommended. Do not increase the number or frequency of doses without medical consultation. If recommended dosage does not provide relief of symptoms or symptoms become worse, seek immediate medical attention. While taking VENTOLIN Inhaler, other inhaled drugs should not be used unless prescribed.

See illustrated Patient's Instructions for Use.

Drug Interactions: Other sympathomimetic aerosol bronchodilators should not be used concomitantly with albuterol. If additional adrenergic drugs are to be administered by any route, they should be used with caution to avoid deleterious cardiovascular effects.

Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants because the action of albuterol on the vascular system may be potentiated.

Beta-receptor blocking agents and albuterol inhibit the effect of each other.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Albuterol sulfate, like other agents in its class, caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium in a two-year study in the rat, at doses corresponding to 111, 555, and 2,800 times the maximum human inhalational dose. In another study this effect was blocked by the coadministration of propranolol. The relevance of these findings to humans is not known. An 18-month study in mice and a lifetime study in hamsters revealed no evidence of tumorigenicity. Studies with albuterol revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Pregnancy: ***Teratogenic Effects: Pregnancy Category C:*** Albuterol has been shown to be teratogenic in mice when given in doses corresponding to 14 times the human dose. There are no adequate and well-controlled studies in pregnant women. Albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A reproduction study in CD-1 mice given albuterol subcutaneously (0.025, 0.25, and 2.5 mg/kg, corresponding to 1.4, 14, and 140 times the maximum human inhalational dose, respectively) showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg. None was observed at 0.025 mg/kg. Cleft palate also occurred in 22 of 72 (30.5%) fetuses treated with 2.5 mg/kg isoproterenol (positive control). A reproduction study with oral albuterol in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) fetuses at 50 mg/kg, corresponding to 2,800 times the maximum human inhalational dose of albuterol.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children below 12 years of age have not been established.

ADVERSE REACTIONS: The adverse reactions to albuterol are similar in nature to reactions to other sympathomimetic agents, although the incidence of certain cardiovascular effects is less with albuterol. A 13-week double-blind study compared albuterol and isoproterenol aerosols in 147 asthmatic patients. The results of this study showed that the incidence of cardiovascular effects was: palpitations, less than 10 per 100 with albuterol and less than 15 per 100 with isoproterenol; tachycardia, 10 per 100 with both albuterol and isoproterenol; and increased blood pressure, less than 5 per 100 with both albuterol and isoproterenol. In the same study, both drugs caused tremor or nausea in less than 15 patients per 100, and dizziness or heartburn in less than 5 per 100 patients. Nervousness occurred in less than 10 per 100 patients receiving albuterol and in less than 15 per 100 patients receiving isoproterenol.

Rare cases of urticaria, angioedema, rash, bronchospasm, and oropharyngeal edema have been reported after the use of inhaled albuterol.

In addition, albuterol, like other sympathomimetic agents, can cause adverse reactions such as hypertension, angina, vomiting, vertigo, central nervous system stimulation, insomnia, headache, unusual taste, and drying or irritation of the oropharynx.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

Allen & Hanburys™
DIVISION OF GLAXO INC.
Research Triangle Park, NC 27709

RB2-211
February 1988

For full Prescribing Information, please consult package insert.

THE "BONE BANK" AN INVESTMENT IN THE FUTURE

Calcium: a disappearing element

Higher calcium intake is indicated during preadolescence and puberty than during childhood because of the demands of rapid skeletal growth.[1] Nevertheless, with the increasing popularity of carbonated drinks and so-called junk food over recent years, as well as peer pressure among females to be thin, many adolescents and preadolescents may not consume all the calcium they need. For example, a U.S. government study[2] found that the mean daily calcium intake for girls 12 to 14 years of age was 72% of the RDA, which is 1,200 mg per day.[3] The intake for girls aged 15 to 17 was even less—only 64% of the RDA.

Calcium in adolescence to build and maintain the "bone bank"

Calcium consumed during adolescence may also have far-reaching consequences throughout life, since both men and women lose bone mass with age.[4,5] To build and maintain an adequate "bone bank," it is logical to begin osteoporosis prevention programs, which include adequate calcium intake, during the active bone-forming years in both sexes.[4,5] A recent study has indicated, for example, that higher milk consumption through adolescence may be associated with greater bone density in the later decades.[6]

Dairy products...versatile calcium source

Since dairy products are the chief source of calcium in the American food supply,[7] and since they are available in a wide variety of good-tasting forms with different fat contents to meet the needs of different patients, it makes excellent sense to recommend dairy products to adolescent and preadolescent patients as their major dietary source of calcium. The fat content of available forms of milk, for example, ranges from a trace in skim milk through 1%, 2%, and to at least 3.25% in whole milk. Richer dairy products (eg, cheeses, ice cream) can be consumed in moderation when appropriate. For lactose-intolerant adolescents, yogurt with active cultures or lactose-free dairy products are available.

DAIRY PRODUCTS TO BUILD AND MAINTAIN THE "BONE BANK"

References: 1. Avioli LV, in Goodhart RS, Shils MR (eds): *Modern Nutrition in Health and Disease*, ed 6. Philadelphia, Lea & Febiger, 1980, pp 194-309. 2. *Second National Health and Nutrition Examination Survey (NHANES II). Dietary Intake Source Data: United States, 1976-80.* National Center for Health Statistics, Public Health Service. Washington, DC, U.S. Government Printing Office, March 1983. 3. *Recommended Dietary Allowances*, ed 9. Washington, DC, National Academy of Sciences, 1980. 4. Rubin K: *Pediatr By-Line* 1985;4(3):1,4-6. 5. Heidrich F, Thompson RS: *J Fam Pract* 1987;25(1):33-39. 6. Sandler RB, Slemenda CW, LaPorte RE, et al: *Am J Clin Nutr* 1985;42:270-274. 7. Marston R, Raper N: *National Food Review* 1987;36:18-23.

Some valuable information for your patients

If you would like a free kit containing patient education materials on dairy calcium's role in adolescent nutrition, please clip and mail this coupon to: Adolescent Nutrition, National Dairy Board, P.O. Box 1063, Fairview, NJ 07022-9763. Please print or type.

Name_____

Specialty_____

Address_____

City_____ State_____ Zip_____

PED 10/88

"One two. Buckle my shoe. Three four...."

Suddenly, no more.

Absence seizures don't last very long. But they disrupt the child's school performance so that teachers may think of these children as "inattentive."

Once simple absence seizures are diagnosed, ZARONTIN® (ethosuximide) is the drug of choice for treatment. ZARONTIN has a well-known safety record and has been generally well tolerated. Hepatic toxicity has not been reported.*

Since ZARONTIN has a specific anti-absence seizure effect, it will not mask generalized tonic-clonic activity. More than two decades of clinical experience have helped ZARONTIN earn its reputation.

ZARONTIN®

(ethosuximide, USP)

Capsules 250mg—Syrup 250mg/5mL

The drug of choice[1-3] for absence (petit mal) seizures

*Minor alterations have been observed in some hepatic and renal function tests. Ethosuximide should therefore be administered with extreme caution to patients with known hepatic or renal disease.

REFERENCES: 1. Wilder BJ, Bruni J: *Seizure Disorders: A Pharmacological Approach to Treatment.* New York, Raven Press, 1981, p 98. 2. Green JB: Epilepsy in adolescents and adults, in Conn HF (ed): *Current Therapy 1982.* Philadelphia, WB Saunders Co, 1982, pp 720-726. 3. Fernandez RJ, Samuels MA: Epilepsy, in Samuels MA (ed): *Manual of Neurologic Therapeutics with Essentials of Diagnosis.* Boston, Little Brown & Co, 1981, pp 75-117.

PARKE-DAVIS

Please see next page for brief summary of prescribing information.

ZARONTIN® (ethosuximide capsules, USP)

Before prescribing, please see full prescribing information.
A Brief Summary follows.

INDICATION: Zarontin is indicated for the control of absence (petit mal) epilepsy.
CONTRAINDICATION: Ethosuximide should not be used in patients with a history of hypersensitivity to succinimides.
WARNINGS: Blood dyscrasias, including some with fatal outcome, have been reported to be associated with the use of ethosuximide; therefore, periodic blood counts should be performed.

Ethosuximide is capable of producing morphological and functional changes in the animal liver. In humans, abnormal liver and renal function studies have been reported.

Ethosuximide should be administered with extreme caution to patients with known liver or renal disease. Periodic urinalysis and liver function studies are advised for all patients receiving the drug.

Cases of systemic lupus erythematosus have been reported with the use of ethosuximide. The physician should be alert to this possibility.

Usage in Pregnancy: The effects of Zarontin in human pregnancy and nursing infants are unknown.

Recent reports suggest an association between the use of anticonvulsant drugs by women with epilepsy and an elevated incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital, but these are also the most commonly prescribed anticonvulsants; less systematic or anecdotal reports suggest a possible similar association with the use of all known anticonvulsant drugs.

The reports suggesting an elevated incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic methodologic problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors, eg, genetic factors or the epileptic condition itself, may be more important than drug therapy in leading to birth defects. The great majority of mothers on anticonvulsant medication deliver normal infants. It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or fetus.

The prescribing physician will wish to weigh these considerations in treating or counseling epileptic women of childbearing potential.

Hazardous Activities: Ethosuximide may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a motor vehicle or other such activity requiring alertness; therefore, the patient should be cautioned accordingly.
PRECAUTIONS: Ethosuximide, when used alone in mixed types of epilepsy, may increase the frequency of grand mal seizures in some patients.

As with other anticonvulsants, it is important to proceed slowly when increasing or decreasing dosage, as well as when adding or eliminating other medication. Abrupt withdrawal of anticonvulsant medication may precipitate absence (petit mal) status.
ADVERSE REACTIONS: Gastrointestinal System: Gastrointestinal symptoms occur frequently and include anorexia, vague gastric upset, nausea and vomiting, cramps, epigastric and abdominal pain, weight loss, and diarrhea.

Hemopoietic System: Hemopoietic complications associated with the administration of ethosuximide have included leukopenia, agranulocytosis, pancytopenia, aplastic anemia, and eosinophilia.

Nervous System: Neurologic and sensory reactions reported during therapy with ethosuximide have included drowsiness, headache, dizziness, euphoria, hiccups, irritability, hyperactivity, lethargy, fatigue, and ataxia. Psychiatric or psychological aberrations associated with ethosuximide administration have included disturbances of sleep, night terrors, inability to concentrate, and aggressiveness. These effects may be noted particularly in patients who have previously exhibited psychological abnormalities. There have been rare reports of paranoid psychosis, increased libido, and increased state of depression with overt suicidal intentions.

Integumentary System: Dermatologic manifestations which have occurred with the administration of ethosuximide have included urticaria, Stevens-Johnson syndrome, systemic lupus erythematosus, and pruritic erythematous rashes.

Miscellaneous: Other reactions reported have included myopia, vaginal bleeding, swelling of the tongue, gum hypertrophy, and hirsutism.

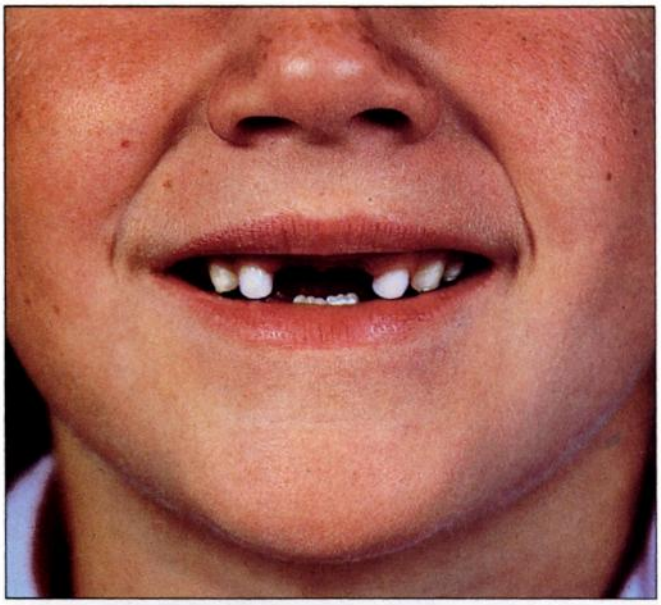
0237GO20

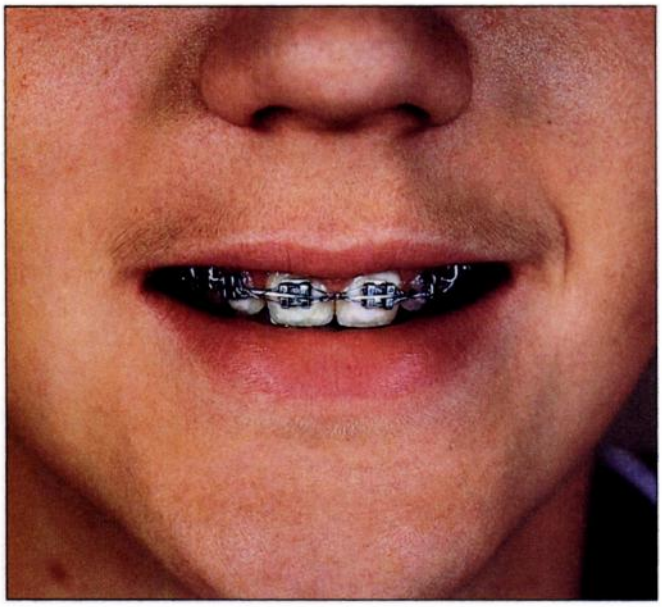
PARKE-DAVIS
Division of Warner-Lambert Company
Morris Plains, New Jersey 07950

PD-12-JA-1790-P-1(9-83)

Stop the pain.

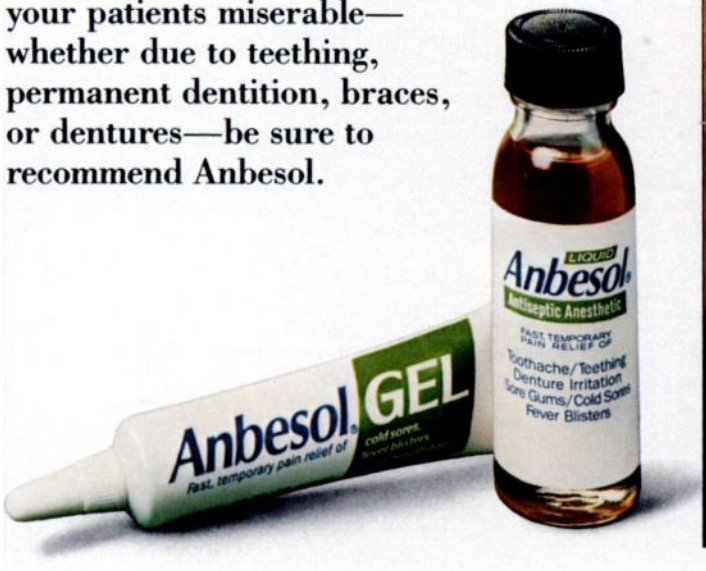
Restore the smiles.

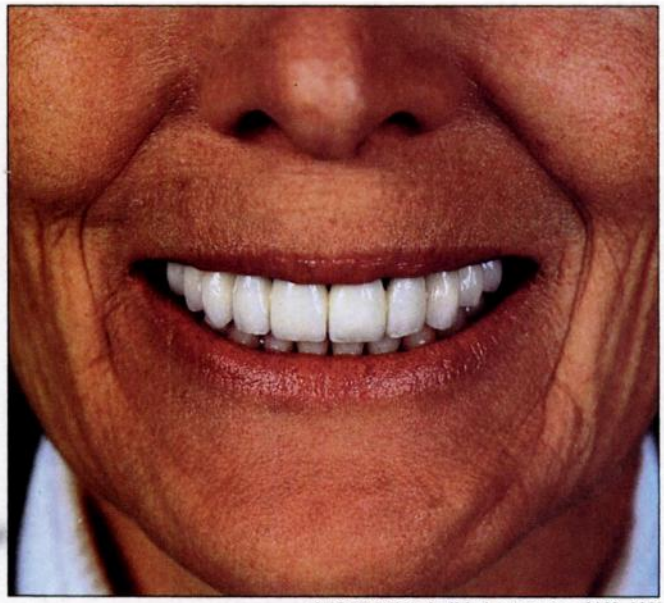




ANBESOL® contains two anesthetics—phenol and benzocaine—that work together to rapidly relieve minor mouth pain. Plus two antiseptics to help prevent infection and promote healing.

So next time minor mouth pain makes your patients miserable—whether due to teething, permanent dentition, braces, or dentures—be sure to recommend Anbesol.





CLUSTERS PROBLEM

"The study could neither confirm nor deny a link between the leukemia incidents and proximity of nuclear power plants because such statistical studies, by their nature, cannot prove cause and effect." So many scientific papers end with these words. It is as if Sherlock Holmes were going out with a shattered magnifying glass and then assiduously reported that he could not see anything.

The problem is not the intention, but the tool. A cluster is a mysterious grouping of disease, in place or time, possibly a fluke and possibly statistically "real"—that is, not due to chance alone. Statistics can determine the "real" clusters but not what the cause may be.

By definition, a statistical study sniffs at a cold trail.

Submitted by Student

From DiPerna P: Futility at the National Cancer Institute. *The New York Times*, March 5, 1988.

UNWANTED CHILDREN

Infant mortality was significantly higher among unwanted children [in Finland] than among the desired children (24.0 *vs* 14.2 per 1000) but no difference was found among the older children up to the age of 16. The incidence of CP and mental retardation (I.Q. <71) up to the age of 14 years was 3.1 and 3.2 times higher in the unwanted children than in the desired children respectively, the differences being statistically highly significant.

Submitted by Student

From Rantakallio P: The longitudinal study of the northern Finland birth cohort of 1966. *Paediatr Perinatol Epidemiol* 1988;2:59–88.

Treating a cold can be as easy as getting one.

Easy for kids to take:
The pleasant cherry-flavored liquids or fruit chewables encourage young patient compliance.

Easy for you to select therapy:
Each PediaCare product treats specific symptoms*... and clearly labeled packaging makes it easy for parents to find.

Easy for parents to give:
The calibrated cup or dropper makes it easy to dose correctly.

*PediaCare Cold Formula contains pseudoephedrine HCl (15 mg/5 ml) and chlorpheniramine maleate (1 mg/5 ml); PediaCare Cough-Cold Formula contains dextromethorphan HBr (5 mg/5 ml), pseudoephedrine HCl (15 mg/5 ml), and chlorpheniramine maleate (1 mg/5 ml), and is available in liquid and chewable tablet forms. PediaCare Oral Decongestant Drops contain pseudoephedrine HCl (7.5 mg/0.8 ml).

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PediaCare™
Children's Cold Relief
Easy for parents...and you.

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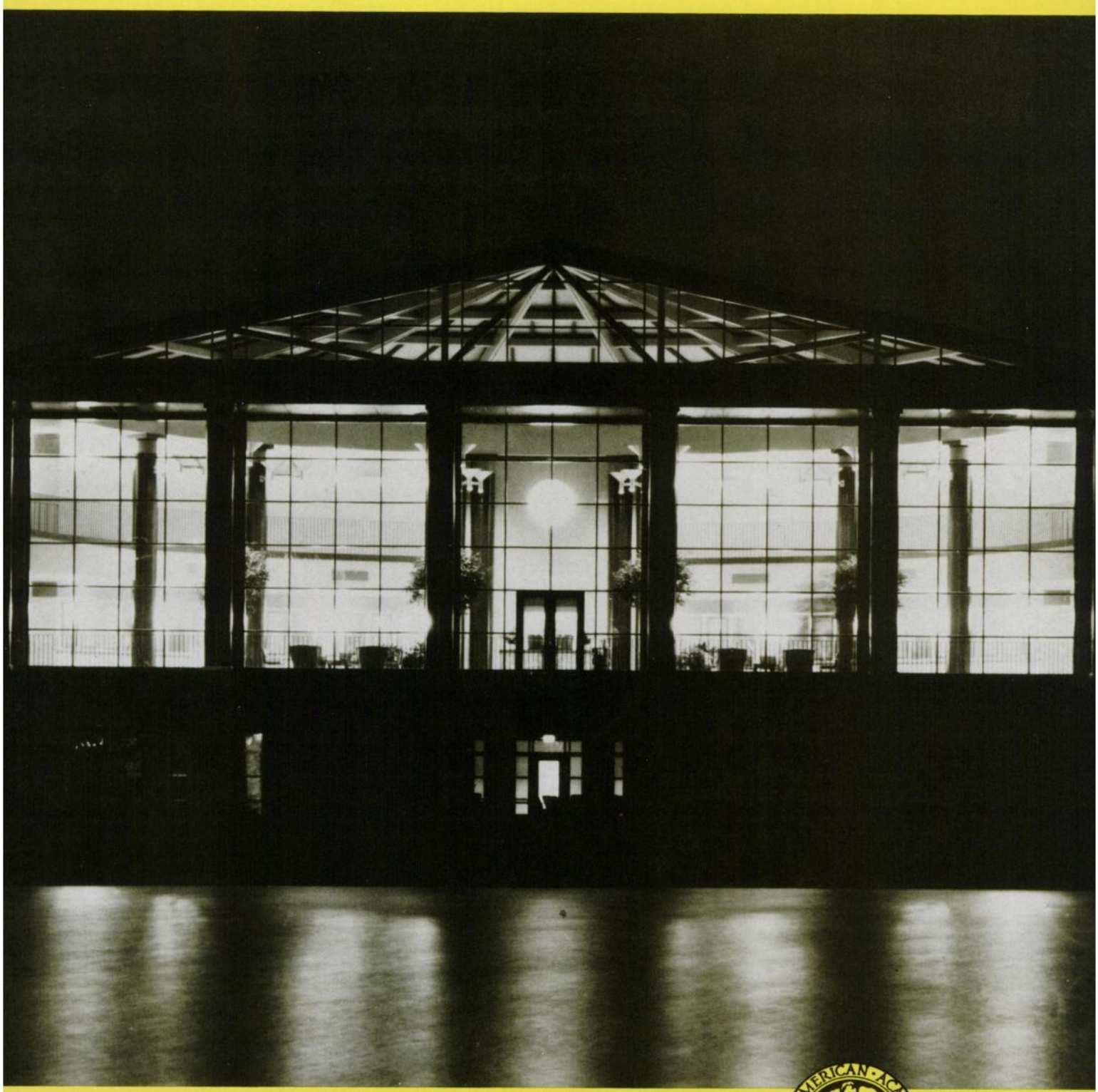

Nightlight view of Academy's national headquarters, from across the lagoon.

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*Read the prospectus before investing or forwarding funds.

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American Academy of Pediatrics

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1989 Spring Session
March 11 – 16

Orlando, sun-kissed playground of the South, beckons you with its magic and merriment. Discover a world of wonder and enchantment in Walt Disney World and Epcot Center. Explore new frontiers at NASA's Spaceport USA, or delight in the antics of marine life at Sea World. Explore the many worlds of Orlando during the American Academy of Pediatrics 1989 Spring Session, March 11-16.

The AAP Spring Session will expand your knowledge and sharpen your skills through plenary sessions, seminars, workshops, section meetings, and special presentations focused on the many health care issues facing pediatricians today. AIDS and Sexually Transmitted Diseases, Immunology, Infectious Diseases, Neonatology and Sports Medicine are just a sampling of the diversified scientific programs available to you.

"New Options for Pediatric Practice," a Special Presentation being held on Wednesday, March 15, will explore alternatives to the standard "full-time" pediatric practice.

Distinguished faculty includes:

Samuel L. Katz, MD, FAAP, *Wilburt Cornell Davison Professor of Pediatrics, Duke University School of Medicine, Durham, North Carolina*

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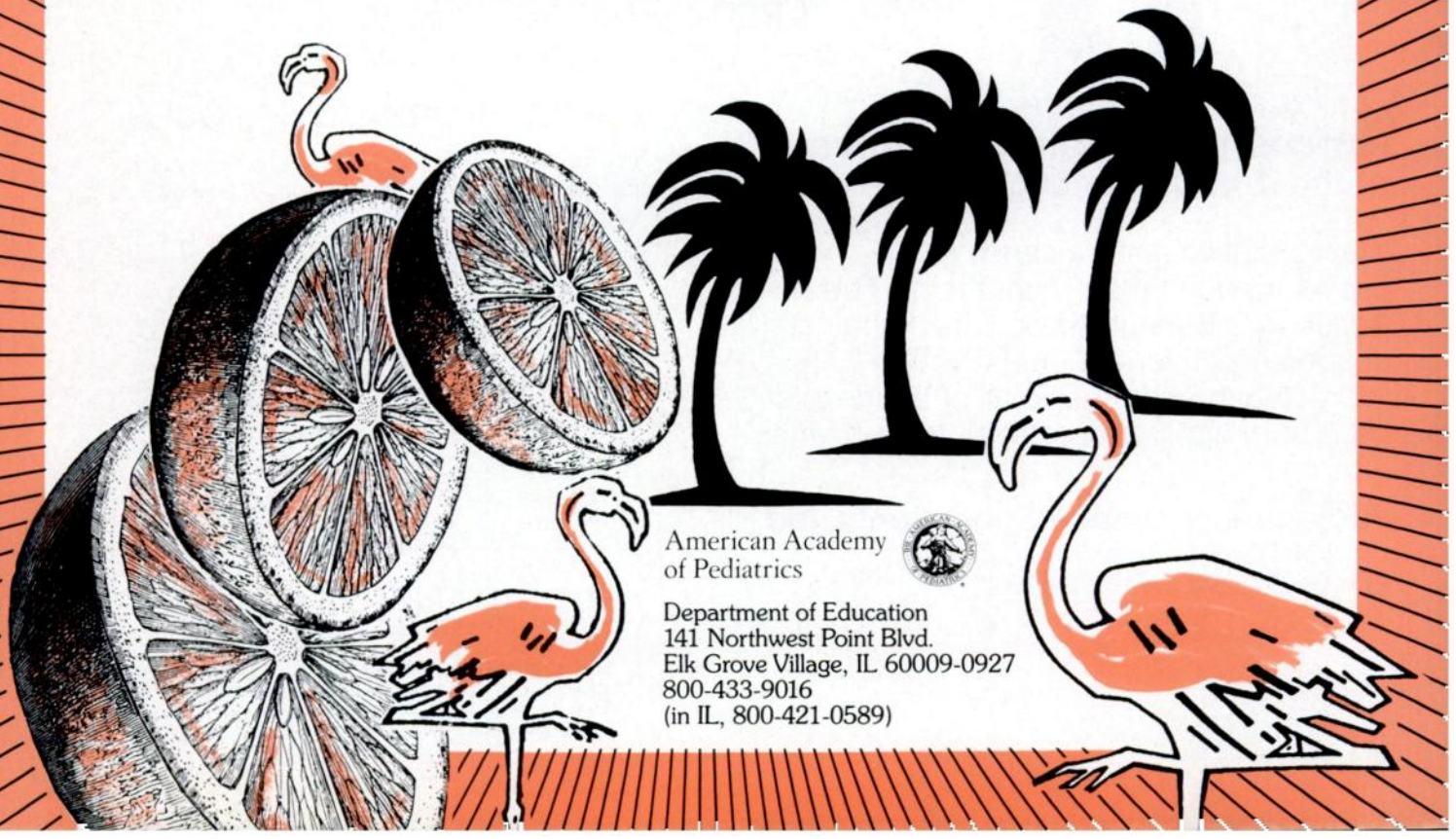
James A. Stockman III, MD, *Physician-in-Chief, Children's Memorial Hospital, Professor and Chairman, Department of Pediatrics, Northwestern University Medical School, Chicago, Illinois*

...plus many other expert faculty.

Build a stronger future for our children.
Join the American Academy of Pediatrics in Orlando, March 11 – 16, 1989.



American Academy of Pediatrics

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SEE WHAT'S NEW!
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AAP Fall Meeting

Think of it as two kinds of relief

One for colds

Like all Triaminic® products, Triaminicol® starts with a proven decongestant to reduce nasal and sinus congestion.

In addition, Triaminicol contains an effective antihistamine to dry runny noses and itchy, watery eyes.

And one for coughs

To stop coughs cold, Triaminicol contains dextromethorphan, a centrally acting antitussive that is non-narcotic, but equally as effective as codeine.[1-3†]

And Triaminicol does it all *without analgesics or alcohol.*

#1 PEDIATRICIAN RECOMMENDED

Triaminicol®
MULTI-SYMPTOM COLD SYRUP

For the cold with a cough

†Except in severe cough

REFERENCES

1. Decongestant, Cough and Cold Preparations in *Drug Evaluations*, ed 6. Chicago, American Medical Association, 1986; pp 374 and 384.
2. Geller RJ, Fisher JG: The role of symptomatic therapy for the common cold. *J Respir Dis* 1987;8(1):20-34.
3. Medon PJ, Holshouser MH: Self Medication: Antitussives. *Pharm Times* 1985;51(1):80-90.

SANDOZ PHARMACEUTICALS CORPORATION
Pediatric Division

Help make the common cold less common.

Recent research indicates: Colds are "caught"...by hand.

Today we know that we are far more likely to catch a cold from our fingers than from a sneeze or a cough.[1] Rhinovirus on a cold sufferer's hands can be easily passed on to other hands. And when contaminated fingers probe a nose or rub an eye, the result is often a common cold infection.

The importance of fomites is more clearly understood.

Contaminated surfaces—or fomites—also help to transmit common cold infections. When a child touches a fomite (which could be a favorite toy), and then goes on to touch his eyes or nose...a cold may follow.

Lysol® Spray: Meets the need for a virucidal agent...

Some experts recommend the use of a virucidal agent to help curb the spread of rhinovirus from fomites to fingers.[1,2] In laboratory studies with human volunteers, LYSOL Spray has been shown to virtually eliminate rhinovirus when applied to contaminated surfaces.[3]

Works to interrupt the chain of transmission

In separate tests involving human volunteers, the use of LYSOL Spray on contaminated tiles actually resulted in a *21% reduction* in common cold infections.[4]

Lysol® Spray: An important part of a patient prevention program

Throughout the year—and *especially* at the first sign of a cold—recommend frequent hand washing...avoidance of finger-to-eye and finger-to-nose contact...and widespread use of LYSOL Spray—to help eliminate rhinovirus on household surfaces, help make the common cold less common.

Please send me a free copy of the informative patient booklet, "Common Cold Facts," to review for use in my practice.

Mail to: Lysol® Common Colds Fact Book, P.O. Box 5440, Westbury, NY 11592

Name _____

Address _____

City _____ State _____ Zip _____

Offer Expires 8/31/89

References:

1. Turner R, Hendley JO: How colds spread: Surprising new data. *J Resp Dis* 1982; 3:98.
2. Klumpp TG: The common cold: New concepts of transmission and prevention. *Med Times* 1980; 108:35.
3. Data on file, Sterling-Winthrop Research Institute, 1977-79.
4. Gwaltney JM Jr, Hendley JO: Transmission of experimental rhinovirus infection by contaminated surfaces. *Am J Epidemiol* 1982;116:828-833.

TIME-OUT FOR TUSSI-ORGANIDIN®

CONTROL COUGHS AT 2 SITES

AT THE COUGH CENTER
Control with your choice of antitussives:
- dextromethorphan
- codeine

AT THE ORIGIN
Moisturize with a mucolytic-expectorant for cough caused by:
- mucus or
- irritation

TUSSI-ORGANIDIN® contains © Codeine

LIQUID Each teaspoonful (5 ml) contains: ORGANIDIN® (iodinated glycerol containing 15 mg organically bound iodine), 30 mg; codeine phosphate (WARNING: May be habit-forming), 10 mg

TUSSI-ORGANIDIN® DM

LIQUID Each teaspoonful (5 ml) contains: ORGANIDIN® (iodinated glycerol containing 15 mg organically bound iodine), 30 mg; dextromethorphan hydrobromide, 10 mg

Dual-Action Cough Control

Please see the following page for a brief summary of prescribing information.

WALLACE LABORATORIES
Division of Carter-Wallace, Inc.
Cranbury, New Jersey 08512

TUSSI-ORGANIDIN®/
TUSSI-ORGANIDIN® DM
Combined Brief Summary

Based on INS ORF08-4/84

Before prescribing, please consult complete product information, a brief summary of which follows:

INDICATIONS AND USAGE: For the symptomatic relief of irritating, nonproductive cough associated with respiratory tract conditions such as chronic bronchitis, bronchial asthma, tracheobronchitis, and the common cold; also for the symptomatic relief of cough accompanying other respiratory tract conditions such as laryngitis, pharyngitis, croup, pertussis and emphysema. Appropriate therapy should be provided for the primary disease.

CONTRAINDICATIONS: History of marked sensitivity to inorganic iodides; hypersensitivity to any of the ingredients or related compounds; pregnancy; newborns; and nursing mothers.

WARNINGS: Discontinue use if rash or other evidence of hypersensitivity appears. Use with caution or avoid use in patients with history or evidence of thyroid disease.

PRECAUTIONS: *General*—Iodides have been reported to cause a flare-up of adolescent acne. Children with cystic fibrosis appear to have an exaggerated susceptibility to the goitrogenic effects of iodides.

Dermatitis and other reversible manifestations of iodism have been reported with chronic use of inorganic iodides. Keep these in mind in patients receiving these preparations for prolonged periods.

Drug Interactions—Iodides may potentiate the hypothyroid effect of lithium and other antithyroid drugs.

Carcinogenesis, Mutagenesis, Impairment of Fertility—No long-term animal studies have been performed.

Pregnancy—Teratogenic effects: Pregnancy Category X (see CONTRAINDICATIONS).

Nursing Mothers—Do not administer to a nursing woman.

ADVERSE REACTIONS: Side effects have been rare, including those which may occur with the individual ingredients and which may be modified as a result of their combination. *Organidin*—Gastrointestinal irritation, rash, hypersensitivity, thyroid gland enlargement, and acute parotitis. *Codeine*—(Tussi-Organidin only): Nausea, vomiting, constipation, drowsiness, dizziness and miosis. *Dextromethorphan*—(Tussi-Organidin DM only): Drowsiness or gastrointestinal disturbances.

DRUG ABUSE AND DEPENDENCE (Tussi-Organidin only):
Controlled substance—Schedule V.
Dependence—Codeine may be habit-forming.

The following sections are optional:
OVERDOSAGE: No reports of any serious problems.

DOSAGE AND ADMINISTRATION
Adults: 1 to 2 teaspoonfuls every 4 hours.
Children: ½ to 1 teaspoonful every 4 hours.

HOW SUPPLIED: *Tussi-Organidin Liquid*—clear red liquid, in bottles of one pint (NDC 0037-4812-10) and one gallon (NDC 0037-4812-20).

Tussi-Organidin DM Liquid—clear yellow liquid, in bottles of one pint (NDC 0037-4712-10) and one gallon (NDC 0037-4712-20).

Storage: Store at room temperature; avoid excessive heat. Keep bottle tightly closed.

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Manufactured by Denver Chemical (Puerto Rico) Inc.
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WALLACE LABORATORIES
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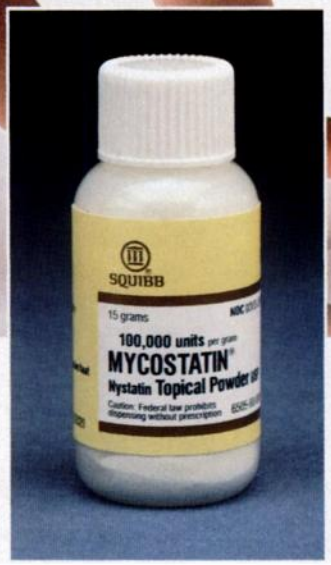
For rapid, safe, symptomatic relief of cutaneous candidiasis

Mycostatin®
Topical Powder
(nystatin topical powder USP)



For a happy ending

- Clinical and mycologic cure in most cases of localized candidiasis
- Virtually nontoxic and nonsensitizing (contains no preservatives)
- Well tolerated by children of all ages—including debilitated infants—even on prolonged administration
- Ideal for moist lesions—an ideal alternative to MYCOSTATIN® Cream (Nystatin Cream) or MYCOSTATIN® Ointment (Nystatin Ointment USP)

MYCOSTATIN® Topical Powder (Nystatin Topical Powder) provides, in every gram, 100,000 units of Nystatin USP dispersed in talc USP.

Supplied in convenient, unbreakable plastic squeeze bottles.

Please see brief summary of prescribing information on adjacent page.

SQUIBB®

698-502

Issued: July 1988

MYCOSTATIN® CREAM
Nystatin Cream

MYCOSTATIN® TOPICAL POWDER
Nystatin Topical Powder

MYCOSTATIN® OINTMENT
Nystatin Ointment USP

DESCRIPTION: Mycostatin Cream contains the antifungal antibiotic Nystatin USP at a concentration of 100,000 units per gram in an aqueous, perfumed vanishing cream base containing aluminum hydroxide concentrated wet gel, titanium dioxide, propylene glycol, cetearyl alcohol (and) ceteareth-20, white petrolatum, sorbitol solution, glyceryl monostearate, polyethylene glycol monostearate, sorbic acid and simethicone.

Mycostatin Topical Powder provides, in each gram, 100,000 units Nystatin USP dispersed in Talc USP.

Mycostatin Ointment provides 100,000 units Nystatin USP per gram in Plastibase® (Plasticized Hydrocarbon Gel), a polyethylene and mineral oil gel base.

INDICATIONS AND USAGE: Mycostatin topical preparations are indicated in the treatment of cutaneous or mucocutaneous mycotic infections caused by *Candida* (Monilia) *albicans* and other Candida species.

CONTRAINDICATIONS: Mycostatin topical preparations are contraindicated in patients with a history of hypersensitivity to any of their components.

PRECAUTIONS: Should a reaction of hypersensitivity occur the drug should be immediately withdrawn and appropriate measures taken.

ADVERSE REACTIONS: Nystatin is virtually nontoxic and nonsensitizing and is well tolerated by all age groups including debilitated infants, even on prolonged administration. If irritation on topical application should occur, discontinue medication.

For full prescribing information, consult package insert.

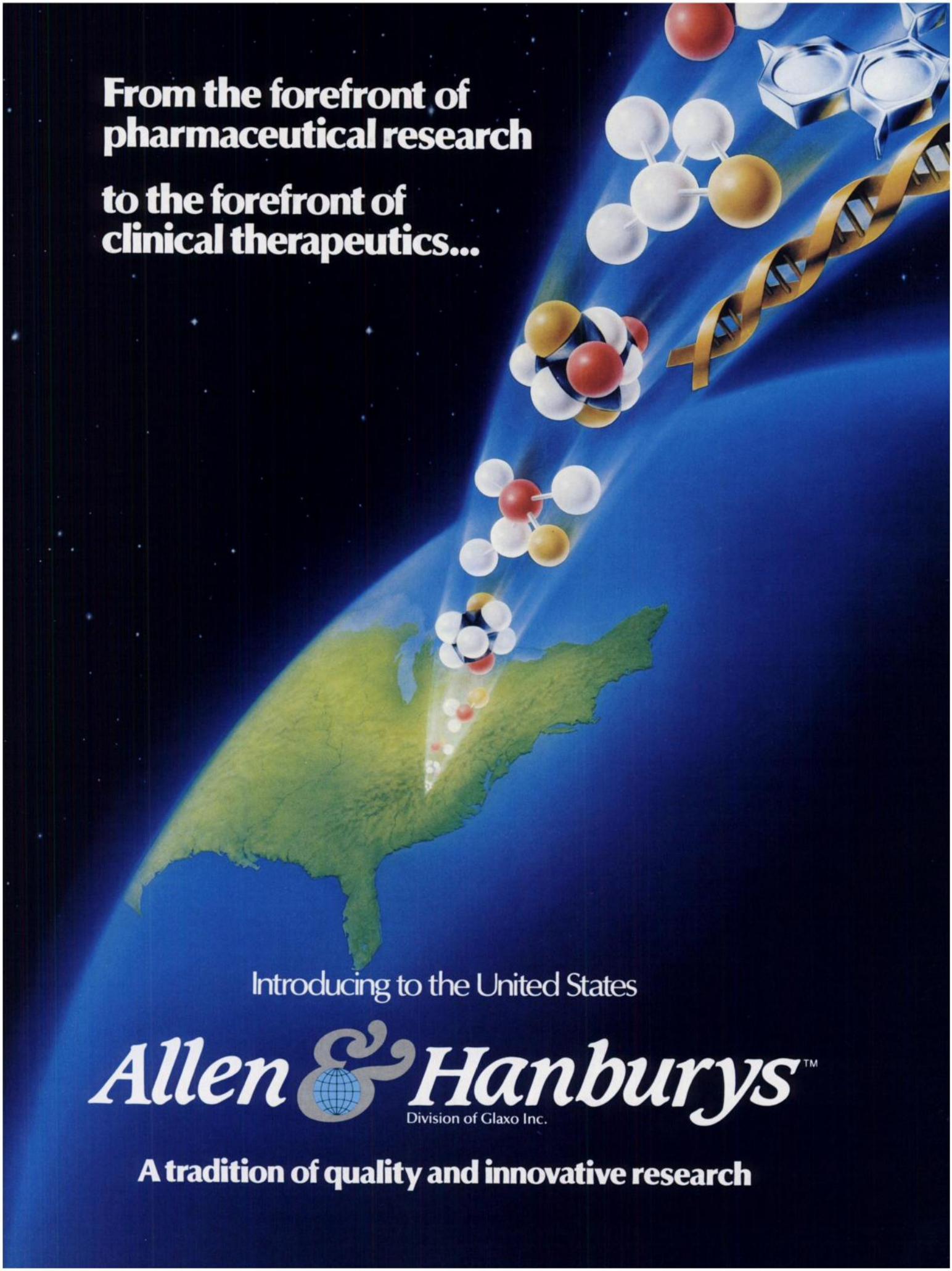
HOW SUPPLIED: Mycostatin Cream (Nystatin Cream) is supplied in tubes providing 100,000 units Nystatin USP per gram in an aqueous, perfumed vanishing cream base.

Mycostatin Topical Powder (Nystatin Topical Powder) is supplied in plastic squeeze bottles providing, in each gram, 100,000 units Nystatin USP.

Mycostatin Ointment (Nystatin Ointment USP) is supplied in tubes providing 100,000 units Nystatin USP per gram.

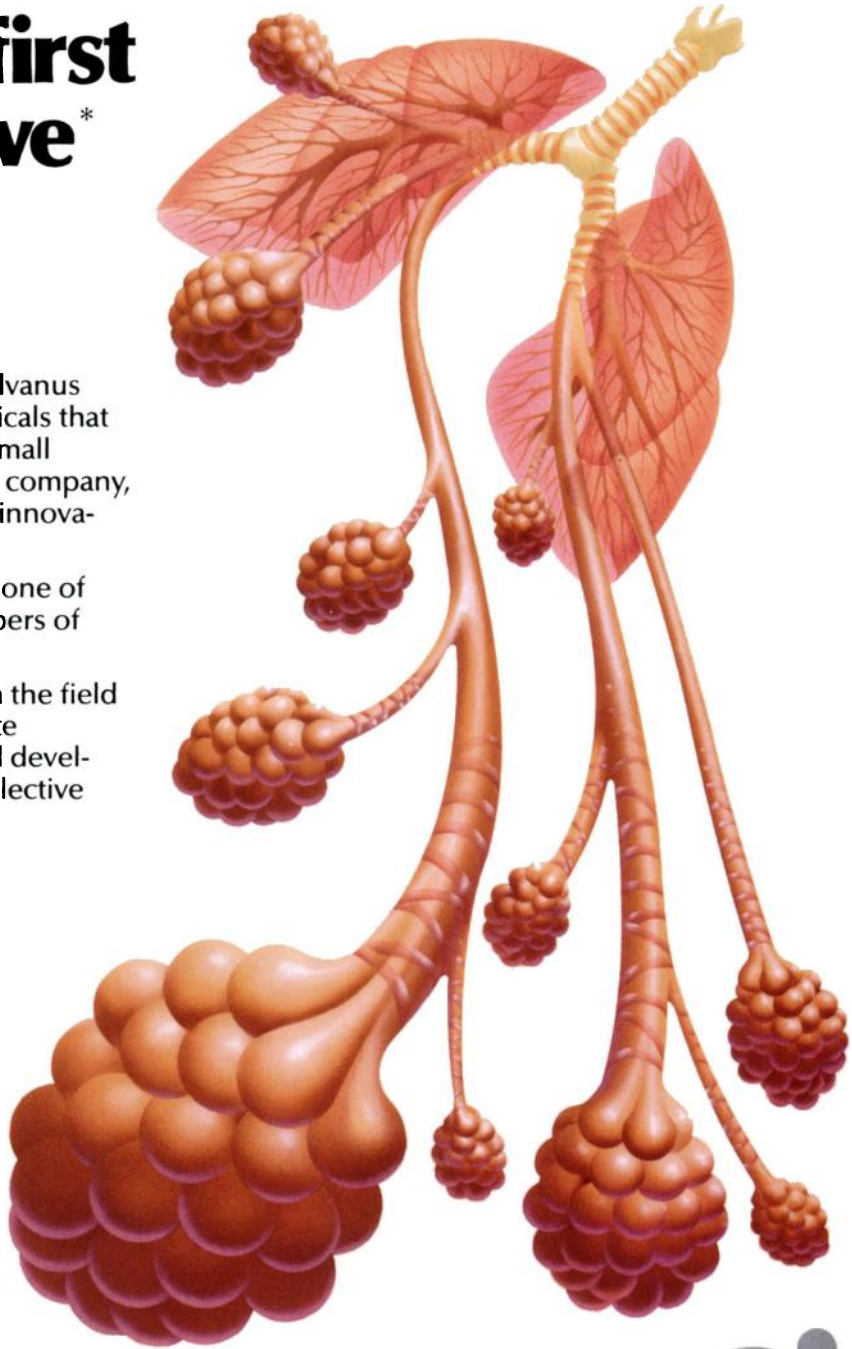
(J3-327A)

698-502 Issued: July 1988


From the forefront of
pharmaceutical research
to the forefront of
clinical therapeutics...
Introducing to the United States
Allen & Hanburys™
Division of Glaxo Inc.
A tradition of quality and innovative research

From innovation in infant formulas in 1892...

to one of the first beta$_2$-selective* stimulants for asthma



In his small, 18th-century apothecary, Silvanus Bevan started a tradition in pharmaceuticals that has continued for over 270 years. That small apothecary has grown into a worldwide company, Allen & Hanburys—and that tradition is innovation.

Innovation has made Allen & Hanburys one of the leading and most progressive members of today's health-care industry.

Recognized as a worldwide innovator in the field of respiratory medicine and receptor-site research, Allen & Hanburys created and developed albuterol—one of the first beta$_2$-selective agonists for asthma.

From the originators of Ventolin® Inhaler†
(albuterol)

Introducing Allen & Hanburys

From innovative research into smallpox inoculation...

to a major advance in corticosteroids

The success of inhaled corticosteroids as a form of therapy is well known. With the development of beclomethasone dipropionate, Allen & Hanburys became a leader in this field. Today, beclomethasone dipropionate is the most widely prescribed intranasal corticosteroid for relief of allergic rhinitis.

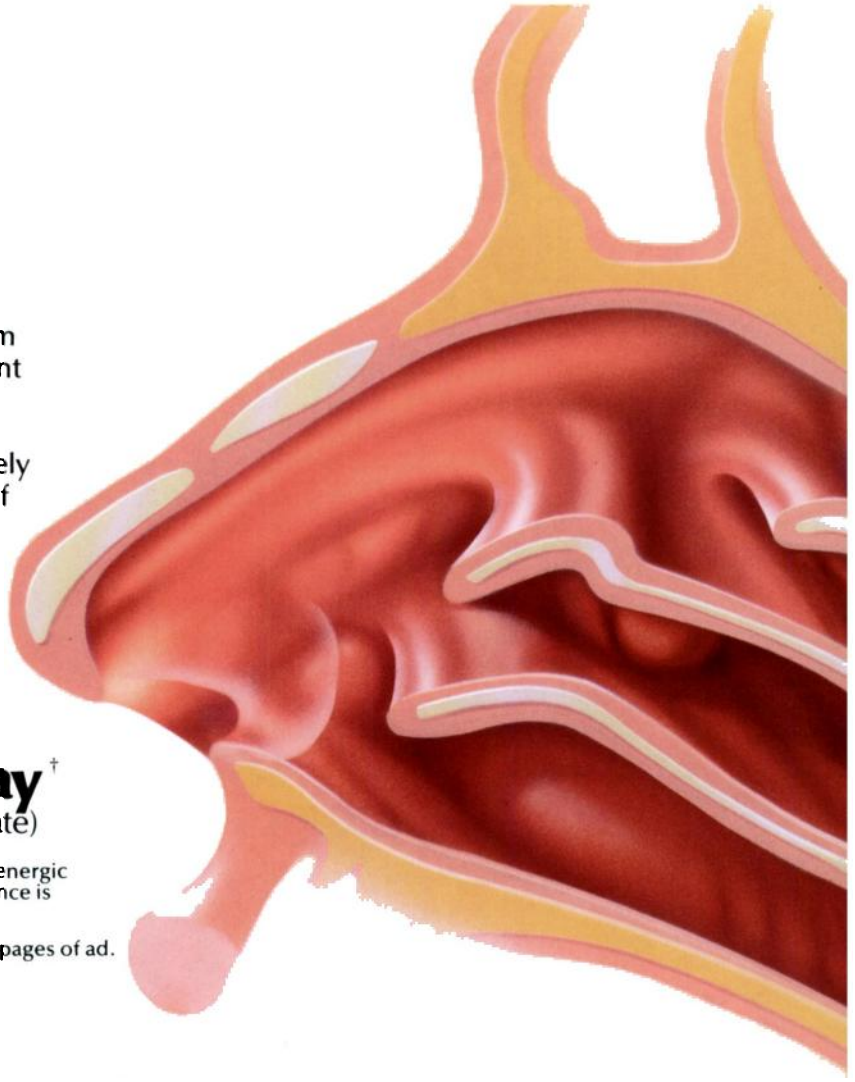
From the originators of Beconase® Nasal Inhaler†
(beclomethasone dipropionate, USP)

and

Beconase AQ® Nasal Spray†
(beclomethasone dipropionate, monohydrate)

*Bronchoselectivity denotes a relative preference for beta$_2$-adrenergic receptors, located chiefly in the bronchial tissue. This preference is not absolute.

†Please see Brief Summaries of Prescribing Information on last pages of ad.



Hanburys
Division of Glaxo Inc.

You know our products.
You know our people and our service.
Now, you know our name.

From innovation in tablet-making machines...

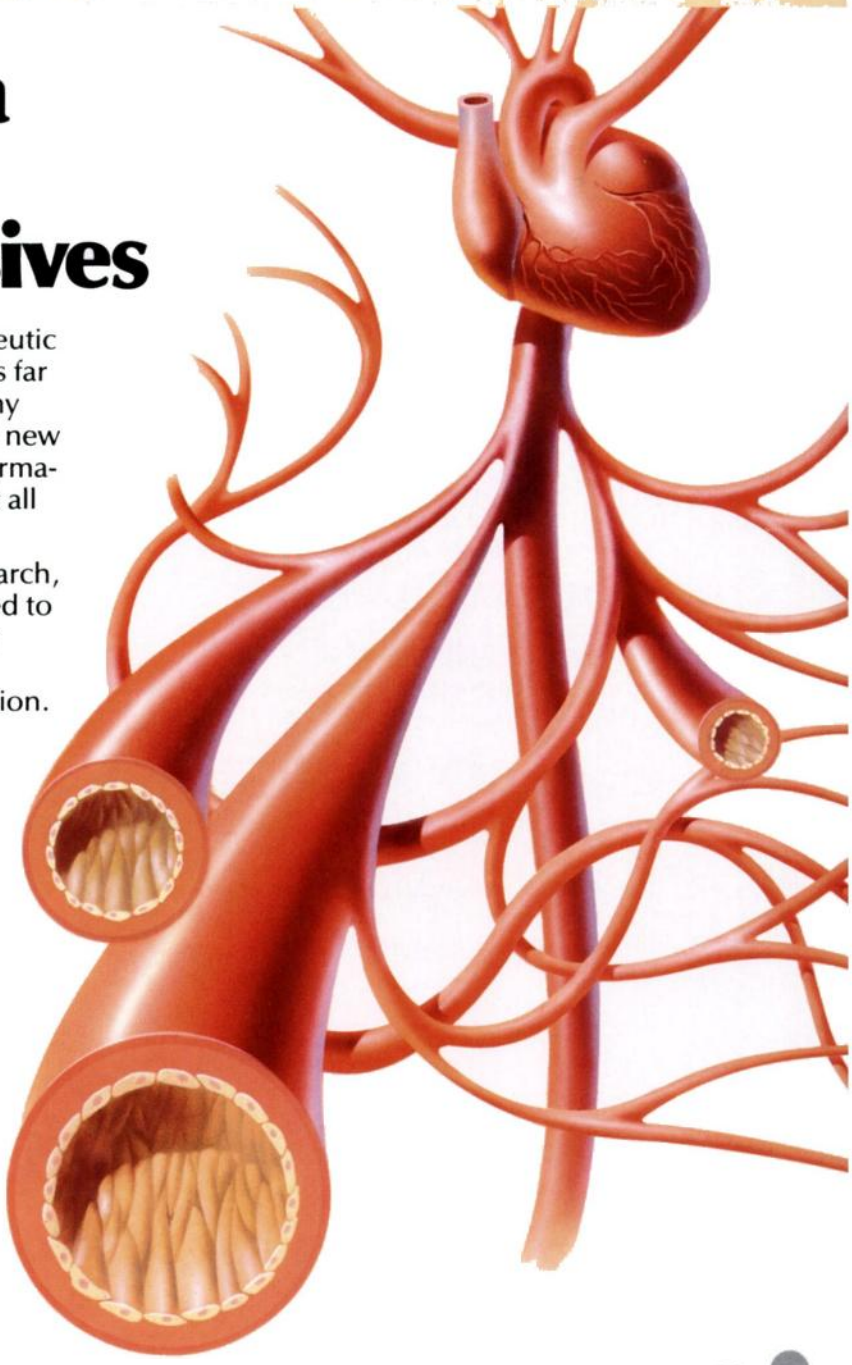
to the first in a new class of antihypertensives

Allen & Hanburys' search for new therapeutic compounds is a commitment that extends far beyond the respiratory field. The company now has 600 scientists abroad engaged in new research, and more than 30 potential pharmaceutical agents are under development at all times.

As a result of extensive receptor-site research, labetalol HCl (TRANDATE®)* tablets proved to be a major contribution to cardiovascular medicine, offering physicians a new therapeutic class for control of hypertension.

From the originators of Trandate® Tablets

(labetalol HCl)



Introducing Allen &

From innovation in cod liver oil processing in the 1840s...

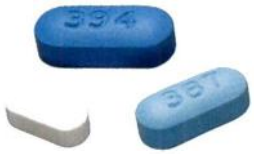
to the broadest in vitro† spectrum oral cephalosporin

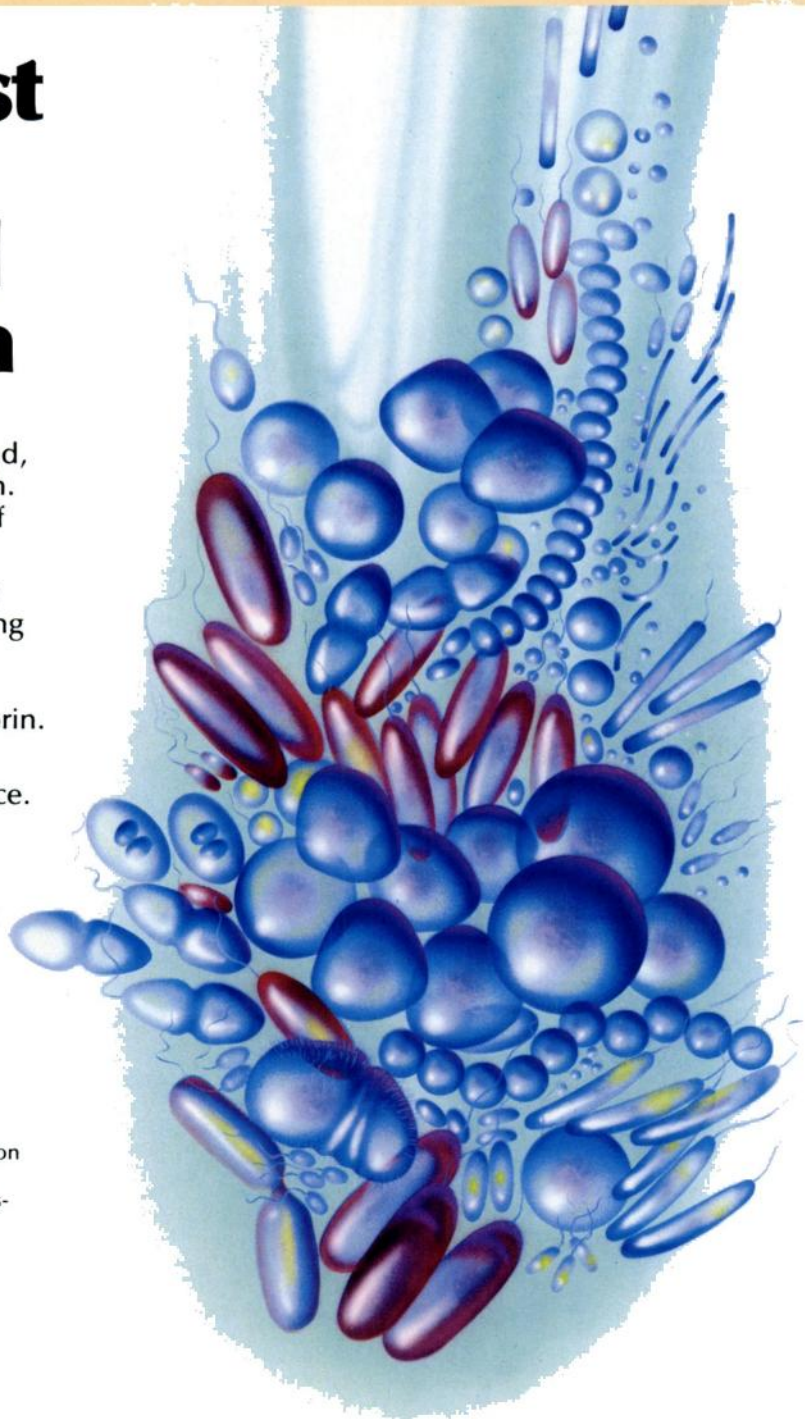
The original site of Allen & Hanburys' research division in Hertfordshire, England, is still the center of Glaxo Group Research. Now, in the United States, our tradition of innovation will continue to flourish.

Among the many breakthroughs of Glaxo Group research is an antibiotic that is being prescribed more and more—CEFTIN® (cefuroxime axetil).* It has the broadest in vitro† spectrum of any oral cephalosporin.

At Allen & Hanburys, the traditions continue. Innovation. Quality. Science. Service. You will soon come to know them all.

Now bringing you Ceftin® (cefuroxime axetil)





*Please see Brief Summaries of Prescribing Information on last pages of ad.

†Although a useful guide, in vitro activity does not necessarily correlate with clinical response.

Hanburys
Division of Glaxo Inc.

You know our products.
You know our people and our service.
Now, you know our name.

VENTOLIN® Inhaler **BRIEF SUMMARY**
(albuterol)

Bronchodilator Aerosol
For Oral Inhalation Only

The following is a brief summary only. Before prescribing, see complete prescribing information in VENTOLIN® Inhaler product labeling.

CONTRAINDICATIONS: VENTOLIN® Inhaler is contraindicated in patients with a history of hypersensitivity to any of its components.

WARNINGS: As with other inhaled beta-adrenergic agonists, VENTOLIN® Inhaler can produce paradoxical bronchospasm that can be life-threatening. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted.

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. The exact cause of death is unknown, but cardiac arrest following the unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected.

Immediate hypersensitivity reactions may occur after administration of albuterol inhaler, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema.

The contents of VENTOLIN Inhaler are under pressure. Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 120°F may cause bursting. Never throw container into fire or incinerator. Keep out of reach of children.

PRECAUTIONS: General: Albuterol, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias and hypertension; in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines.

Large doses of intravenous albuterol have been reported to aggravate pre-existing diabetes mellitus and ketoacidosis. Additionally, beta-agonists, including albuterol, given intravenously may cause a decrease in serum potassium, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation. The relevance of these observations to the use of VENTOLIN® Inhaler is unknown, since the aerosol dose is much lower than the doses given intravenously.

Although there have been no reports concerning the use of VENTOLIN Inhaler during labor and delivery, it has been reported that high doses of albuterol administered intravenously inhibit uterine contractions. Although this effect is extremely unlikely as a consequence of aerosol use, it should be kept in mind.

Information for Patients: The action of VENTOLIN Inhaler may last up to six hours, and therefore it should not be used more frequently than recommended. Do not increase the number or frequency of doses without medical consultation. If recommended dosage does not provide relief of symptoms or symptoms become worse, seek immediate medical attention. While taking VENTOLIN Inhaler, other inhaled drugs should not be used unless prescribed.

See illustrated Patient's Instructions for Use.

Drug Interactions: Other sympathomimetic aerosol bronchodilators should not be used concomitantly with albuterol. If additional adrenergic drugs are to be administered by any route, they should be used with caution to avoid deleterious cardiovascular effects.

Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants because the action of albuterol on the vascular system may be potentiated.

Beta-receptor blocking agents and albuterol inhibit the effect of each other.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Albuterol sulfate, like other agents in its class, caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium in a two-year study in the rat, at doses corresponding to 111, 555, and 2,800 times the maximum human inhalational dose. In another study this effect was blocked by the coadministration of propranolol. The relevance of these findings to humans is not known. An 18-month study in mice and a lifetime study in hamsters revealed no evidence of tumorigenicity. Studies with albuterol revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Pregnancy: *Teratogenic Effects: Pregnancy Category C:* Albuterol has been shown to be teratogenic in mice when given in doses corresponding to 14 times the human dose. There are no adequate and well-controlled studies in pregnant women. Albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A reproduction study in CD-1 mice given albuterol subcutaneously (0.025, 0.25, and 2.5 mg/kg, corresponding to 1.4, 14, and 140 times the maximum human inhalational dose, respectively) showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg. None was observed at 0.025 mg/kg. Cleft palate also occurred in 22 of 72 (30.5%) fetuses treated with 2.5 mg/kg isoproterenol (positive control). A reproduction study with oral albuterol in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) fetuses at 50 mg/kg, corresponding to 2,800 times the maximum human inhalational dose of albuterol.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children below 12 years of age have not been established.

ADVERSE REACTIONS: The adverse reactions to albuterol are similar in nature to reactions to other sympathomimetic agents, although the incidence of certain cardiovascular effects is less with albuterol. A 13-week double-blind study compared albuterol and isoproterenol aerosols in 147 asthmatic patients. The results of this study showed that the incidence of cardiovascular effects was: palpitations, less than 10 per 100 with albuterol and less than 15 per 100 with isoproterenol; tachycardia, 10 per 100 with both albuterol and isoproterenol; and increased blood pressure, less than 5 per 100 with both albuterol and isoproterenol. In the same study, both drugs caused tremor or nausea in less than 15 patients per 100, and dizziness or heartburn in less than 5 per 100 patients. Nervousness occurred in less than 10 per 100 patients receiving albuterol and in less than 15 per 100 patients receiving isoproterenol.

Rare cases of urticaria, angioedema, rash, bronchospasm, and oropharyngeal edema have been reported after the use of inhaled albuterol.

In addition, albuterol, like other sympathomimetic agents, can cause adverse reactions such as hypertension, angina, vomiting, vertigo, central nervous system stimulation, insomnia, headache, unusual taste, and drying or irritation of the oropharynx.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

Glaxo Inc., Research Triangle Park, NC 27709 February 1988

BECONASE® Nasal Inhaler **BRIEF SUMMARY**
(beclomethasone dipropionate, USP)
For Nasal Inhalation Only

BECONASE AQ® Nasal Spray, 0.042%* **SHAKE WELL**
(beclomethasone dipropionate, monohydrate) **BEFORE USE.**

For Intranasal Use Only ***Calculated on the dried basis.**

The following is a brief summary only. Before prescribing, see complete prescribing information in BECONASE® Nasal Inhaler and BECONASE AQ® Nasal Spray product labeling.

CONTRAINDICATIONS: Hypersensitivity to any of the ingredients of either preparation contraindicates its use.

WARNINGS: The replacement of a systemic corticosteroid with BECONASE® Nasal Inhaler or BECONASE AQ® Nasal Spray can be accompanied by signs of adrenal insufficiency.

Careful attention must be given when patients previously treated for prolonged periods with systemic corticosteroids are transferred to BECONASE Nasal Inhaler or BECONASE AQ Nasal Spray. This is particularly important in those patients who have associated asthma or other clinical conditions where too rapid a decrease in systemic corticosteroids may cause a severe exacerbation of their symptoms.

Studies have shown that the combined administration of alternate-day prednisone systemic treatment and orally inhaled beclomethasone increases the likelihood of HPA suppression compared to a therapeutic dose of either one alone. Therefore, BECONASE Nasal Inhaler and BECONASE AQ Nasal Spray treatment should be used with caution in patients already on alternate-day prednisone regimens for any disease.

If recommended doses of intranasal beclomethasone are exceeded or if individuals are particularly sensitive or predisposed by virtue of recent systemic steroid therapy, symptoms of hypercorticism may occur, including very rare cases of menstrual irregularities, acneiform lesions, and cushingoid features. If such changes occur, BECONASE Nasal Inhaler and BECONASE AQ Nasal Spray should be discontinued slowly consistent with accepted procedures for discontinuing oral steroid therapy.

PRECAUTIONS: General: During withdrawal from oral steroids, some patients may experience symptoms of withdrawal, eg, joint and/or muscular pain, lassitude, and depression.

Rarely, immediate hypersensitivity reactions may occur after the intranasal administration of beclomethasone.

Extremely rare instances of wheezing, nasal septum perforation, and increased intraocular pressure have been reported following the intranasal application of aerosolized corticosteroids. Although these have not been observed in clinical trials with BECONASE AQ® Nasal Spray, vigilance should be maintained.

In clinical studies with beclomethasone dipropionate administered intranasally, the development of localized infections of the nose and pharynx with *Candida albicans* has occurred only rarely. When such an infection develops, it may require treatment with appropriate local therapy or discontinuation of treatment with BECONASE® Nasal Inhaler or BECONASE AQ Nasal Spray.

If persistent nasopharyngeal irritation occurs, it may be an indication for stopping BECONASE AQ Nasal Spray.

Beclomethasone dipropionate is absorbed into the circulation. Use of excessive doses of BECONASE Nasal Inhaler or BECONASE AQ Nasal Spray may suppress HPA function.

BECONASE Nasal Inhaler and BECONASE AQ Nasal Spray should be used with caution, if at all, in patients with active or quiescent tuberculous infections of the respiratory tract; untreated fungal, bacterial, or systemic viral infections; or ocular herpes simplex.

For either preparation to be effective in the treatment of nasal polyps, the aerosol or spray must be able to enter the nose. Therefore, treatment of nasal polyps with these preparations should be considered adjunctive therapy to surgical removal and/or the use of other medications that will permit effective penetration of these preparations into the nose. Nasal polyps may recur after any form of treatment.

As with any long-term treatment, patients using BECONASE Nasal Inhaler or BECONASE AQ Nasal Spray over several months or longer should be examined periodically for possible changes in the nasal mucosa.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery, or trauma should not use a nasal corticosteroid until healing has occurred.

Although systemic effects have been minimal with recommended doses, this potential increases with excessive doses. Therefore, larger than recommended doses of BECONASE Nasal Inhaler and BECONASE AQ Nasal Spray should be avoided.

Information for Patients: Patients being treated with BECONASE Nasal Inhaler or BECONASE AQ Nasal Spray should receive the following information and instructions. This information is intended to aid in the safe and effective use of medication. It is not a disclosure of all possible adverse or intended effects. Patients should use these preparations at regular intervals since their effectiveness depends on their regular use. The patient should take the medication as directed. It is not acutely effective, and the prescribed dosage should not be increased. Instead, nasal vasoconstrictors or oral antihistamines may be needed until the effects of BECONASE Nasal Inhaler or BECONASE AQ Nasal Spray are fully manifested. One to two weeks may pass before full relief is obtained. The patient should contact the doctor if symptoms do not improve, or if the condition worsens, or if sneezing or nasal irritation occurs. For the proper use of either unit and to attain maximum improvement, the patient should read and follow the accompanying patient's instructions carefully.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Treatment of rats for a total of 95 weeks, 13 weeks by inhalation and 82 weeks by the oral route, resulted in no evidence of carcinogenic activity. Mutagenic studies have not been performed.

Impairment of fertility, as evidenced by inhibition of the estrous cycle in dogs, was observed following treatment by the oral route. No inhibition of the estrous cycle in dogs was seen following treatment with beclomethasone dipropionate by the inhalation route.

Pregnancy: *Teratogenic Effects: Pregnancy Category C:* Like other corticoids, parenteral (subcutaneous) beclomethasone dipropionate has been shown to be teratogenic and embryocidal in the mouse and rabbit when given in doses approximately ten times the human dose. In these studies, beclomethasone was found to produce fetal resorption, cleft palate, agnathia, microstomia, absence of tongue, delayed ossification, and agenesis of the thymus. No teratogenic or embryocidal effects have been seen in the rat when beclomethasone dipropionate was administered by inhalation at ten times the human dose or orally at 1,000 times the human dose. There are no adequate and well-controlled studies in pregnant women. Beclomethasone dipropionate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects: Hypoadrenalism may occur in infants born of mothers receiving corticosteroids during pregnancy. Such infants should be carefully observed.

Nursing Mothers: It is not known whether beclomethasone dipropionate is excreted in human milk. Because other corticosteroids are excreted in human milk, caution should be exercised when BECONASE Nasal Inhaler or BECONASE AQ Nasal Spray is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below 6 years of age have not been established.

ADVERSE REACTIONS: In general, side effects in clinical studies with both preparations have been primarily associated with irritation of the nasal mucous membranes.

Extremely rare instances of wheezing, nasal septum perforation, and increased intraocular pressure have been reported following the intranasal administration of aerosolized corticosteroids (see PRECAUTIONS).

Rare cases of immediate and delayed hypersensitivity reactions, including urticaria, angioedema, rash, and bronchospasm, have been reported following the oral and intranasal inhalation and administration of beclomethasone.

BECONASE® Nasal Inhaler: Adverse reactions reported in controlled clinical trials and long-term open studies are described below. Sensations of irritation and burning in the nose (11 per 100 patients) following the use of BECONASE Nasal Inhaler have been reported. Also, occasional sneezing attacks (10 per 100 adult patients) have occurred immediately following the use of the intranasal inhaler. This symptom may be more common in children. Rhinorrhea may occur occasionally (1 per 100 patients).

Localized infections of the nose and pharynx with *Candida albicans* have occurred rarely (see PRECAUTIONS). Transient episodes of epistaxis have been reported in 2 per 100 patients. Ulceration of the nasal mucosa has been reported rarely.

Systemic corticosteroid side effects were not reported during controlled clinical trials with BECONASE Nasal Inhaler. If recommended doses are exceeded, however, or if individuals are particularly sensitive, symptoms of hypercorticism, ie, Cushing's syndrome, could occur.

BECONASE AQ® Nasal Spray: Adverse reactions reported in controlled clinical trials and open studies are described below.

Mild nasopharyngeal irritation has been reported in up to 24% of patients treated, including occasional sneezing attacks (about 4%) occurring immediately following use of the spray. In patients experiencing these symptoms, none had to discontinue treatment. The incidence of transient irritation and sneezing was approximately the same in the group of patients who received placebo in these studies, implying that these complaints may be related to vehicle components of the formulation.

Fewer than 5 per 100 patients reported headache, nausea, or lightheadedness. Fewer than 3 per 100 patients reported nasal stuffiness, nosebleeds, rhinorrhea, or tearing eyes.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

Glaxo Inc., Research Triangle Park, NC 27709 July 1988

TRANDATE® Tablets **BRIEF SUMMARY**
(labetalol hydrochloride)

The following is a brief summary only. Before prescribing, see complete prescribing information in TRANDATE® Tablets product labeling.

CONTRAINDICATIONS: TRANDATE® Tablets are contraindicated in bronchial asthma, overt cardiac failure, greater-than-first-degree heart block, cardiogenic shock, and severe bradycardia (see WARNINGS).

WARNINGS: Cardiac Failure: Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure. Beta-blockade carries a potential hazard of further depressing myocardial contractility and precipitating more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary, labetalol HCl can be used with caution in patients with a history of heart failure who are well compensated. Congestive heart failure has been observed in patients receiving labetalol HCl. Labetalol HCl does not abolish the inotropic action of digitalis on heart muscle.

In Patients Without a History of Cardiac Failure: In patients with latent cardiac insufficiency, continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or be given a diuretic, and the response should be observed closely. If cardiac failure continues despite adequate digitalization and diuretic, TRANDATE® therapy should be withdrawn (gradually, if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal: Angina pectoris has not been reported upon labetalol HCl discontinuation. However, hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after *abrupt* discontinuation of such therapy. When discontinuing chronically administered TRANDATE, particularly in patients with ischemic heart disease, the dosage should be gradually reduced over a period of one to two weeks and the patient should be carefully monitored. If angina markedly worsens or acute coronary insufficiency develops, TRANDATE administration should be reinstituted promptly, at least temporarily, and other measures appropriate for the management of unstable angina should be taken. Patients should be warned against interruption or discontinuation of therapy without the physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue TRANDATE therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (eg, Chronic Bronchitis and Emphysema): Patients with bronchospastic disease should, in general, not receive beta-blockers. TRANDATE may be used with caution, however, in patients who do not respond to, or cannot tolerate,

other antihypertensive agents. It is prudent, if TRANDATE is used, to use the smallest effective dose, so that inhibition of endogenous or exogenous beta-agonists is minimized.

Pheochromocytoma: Labetalol HCl has been shown to be effective in lowering blood pressure and relieving symptoms in patients with pheochromocytoma. However, paradoxical hypertensive responses have been reported in a few patients with this tumor; therefore, use caution when administering labetalol HCl to patients with pheochromocytoma.

Diabetes Mellitus and Hypoglycemia: Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (eg, tachycardia) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces the release of insulin in response to hyperglycemia; it may therefore be necessary to adjust the dose of antidiabetic drugs.

Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy before major surgery is controversial. Protracted severe hypotension and difficulty in restarting or maintaining a heartbeat have been reported with beta-blockers. The effect of labetalol HCl's alpha-adrenergic activity has not been evaluated in this setting.

A synergism between labetalol HCl and halothane anesthesia has been shown (see PRECAUTIONS: Drug Interactions).

PRECAUTIONS: General: ***Impaired Hepatic Function:*** TRANDATE® Tablets should be used with caution in patients with impaired hepatic function since metabolism of the drug may be diminished.

Jaundice or Hepatic Dysfunction: On rare occasions, labetalol HCl has been associated with jaundice (both hepatic and cholestatic). It is therefore recommended that treatment with labetalol HCl be stopped immediately should a patient develop jaundice or laboratory evidence of liver injury. Both have been shown to be reversible on stopping therapy.

Information for Patients: As with all drugs with beta-blocking activity, certain advice to patients being treated with labetalol HCl is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects. While no incidence of the abrupt withdrawal phenomenon (exacerbation of angina pectoris) has been reported with labetalol HCl, dosing with TRANDATE Tablets should not be interrupted or discontinued without a physician's advice. Patients being treated with TRANDATE Tablets should consult a physician at any sign of impending cardiac failure. Also, transient scalp tingling may occur, usually when treatment with TRANDATE Tablets is initiated (see ADVERSE REACTIONS).

Laboratory Tests: As with any new drug given over prolonged periods, laboratory parameters should be observed over regular intervals. In patients with concomitant illnesses, such as impaired renal function, appropriate tests should be done to monitor these conditions.

Drug Interactions: In one survey, 2.3% of patients taking labetalol HCl in combination with tricyclic antidepressants experienced tremor as compared to 0.7% reported to occur with labetalol HCl alone. The contribution of each of the treatments to this adverse reaction is unknown, but the possibility of a drug interaction cannot be excluded.

Drugs possessing beta-blocking properties can blunt the bronchodilator effect of beta-receptor agonist drugs in patients with bronchospasm; therefore, doses greater than the normal antiasthmatic dose of beta-agonist bronchodilator drugs may be required.

Cimetidine has been shown to increase the bioavailability of labetalol HCl. Since this could be explained either by enhanced absorption or by an alteration of hepatic metabolism of labetalol HCl, special care should be used in establishing the dose required for blood pressure control in such patients.

Synergism has been shown between halothane anesthesia and intravenously administered labetalol HCl. During controlled hypotensive anesthesia using labetalol HCl in association with halothane, high concentrations (3% or above) of halothane should not be used because the degree of hypotension will be increased and because of the possibility of a large reduction in cardiac output and an increase in central venous pressure. The anesthesiologist should be informed when a patient is receiving labetalol HCl.

Labetalol HCl blunts the reflex tachycardia produced by nitroglycerin without preventing its hypotensive effect. If labetalol HCl is used with nitroglycerin in patients with angina pectoris, additional antihypertensive effects may occur.

Drug/Laboratory Test Interactions: The presence of a metabolite of labetalol in the urine may result in falsely increased levels of urinary catecholamines when measured by a nonspecific trihydroxyindole (THI) reaction. In screening patients suspected of having a pheochromocytoma and being treated with labetalol HCl, specific radioenzymatic or high performance liquid chromatography assay techniques should be used to determine levels of catecholamines or their metabolites.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term oral dosing studies with labetalol HCl for 18 months in mice and for two years in rats showed no evidence of carcinogenesis. Studies with labetalol HCl using dominant lethal assays in rats and mice and exposing microorganisms according to modified Ames tests showed no evidence of mutagenesis.

Pregnancy: ***Teratogenic Effects: Pregnancy Category C:*** Teratogenic studies were performed with labetalol in rats and rabbits at oral doses up to approximately six and four times the maximum recommended human dose (MRHD), respectively. No reproducible evidence of fetal malformations was observed. Increased fetal resorptions were seen in both species at doses approximating the MRHD. A teratology study performed with labetalol in rabbits at intravenous doses up to 1.7 times the MRHD revealed no evidence of drug-related harm to the fetus. There are no adequate and well-controlled studies in pregnant women. Labetalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects: Infants of mothers who were treated with labetalol HCl during pregnancy did not appear to be adversely affected by the drug. Oral administration of labetalol to rats during late gestation through weaning at doses of two to four times the MRHD caused a decrease in neonatal survival.

Labor and Delivery: Labetalol HCl given to pregnant women with hypertension did not appear to affect the usual course of labor and delivery.

Nursing Mothers: Small amounts of labetalol (approximately 0.004% of the maternal dose) are excreted in human milk. Caution should be exercised when TRANDATE Tablets are administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Most adverse effects are mild, transient, and occur early in the course of treatment. In controlled clinical

trials of three to four months' duration, discontinuation of TRANDATE® Tablets due to one or more adverse effects was required in 7% of all patients. In these same trials, beta-blocker control agents led to discontinuation in 8% to 10% of patients, and a centrally acting alpha-agonist in 30% of patients.

The following adverse reactions were derived from multicenter, controlled clinical trials over treatment periods of three and four months. The rates, which ranged from less than 1% to 5% except as otherwise noted, are based on adverse reactions considered probably drug-related by the investigator. If all reports are considered, the rates are somewhat higher (eg, dizziness, 20%; nausea, 14%; fatigue, 11%).

Body as a Whole: Fatigue, asthenia, headache. ***Gastrointestinal:*** Nausea (6%), vomiting, dyspepsia, diarrhea, taste distortion. ***Central and Peripheral Nervous Systems:*** Dizziness (11%), paresthesia, drowsiness. ***Autonomic Nervous System:*** Nasal stuffiness, ejaculation failure, impotence, increased sweating. ***Cardiovascular:*** Edema, postural hypotension. ***Respiratory:*** Dyspnea. ***Skin:*** Rash. ***Special Senses:*** Vision abnormality, vertigo.

The adverse effects were reported spontaneously and are representative of the incidence of adverse effects that may be observed in a properly selected hypertensive patient population, ie, a group excluding patients with bronchospastic disease, overt congestive heart failure, or other contraindications to beta-blocker therapy.

Clinical trials also included studies utilizing daily doses up to 2,400 mg in more severely hypertensive patients. The US therapeutic trials data base for adverse reactions that are clearly or possibly dose-related shows that the following side effects increased with increasing dose: dizziness, fatigue, nausea, vomiting, dyspepsia, paresthesia, nasal stuffiness, ejaculation failure, impotence, and edema.

In addition, a number of other less common adverse events have been reported in clinical trials or the literature:

Cardiovascular: Postural hypotension, including, rarely, syncope. ***Central and Peripheral Nervous Systems:*** Paresthesia, most frequently described as scalp tingling. In most cases, it was mild, transient, and usually occurred at the beginning of treatment. ***Collagen Disorders:*** Systemic lupus erythematosus; positive antinuclear factor (ANF). ***Eyes:*** Dry eyes. ***Immunological System:*** Antimitochondrial antibodies. ***Liver and Biliary System:*** Cholestasis with or without jaundice. ***Musculoskeletal System:*** Muscle cramps, toxic myopathy. ***Respiratory System:*** Bronchospasm. ***Skin and Appendages:*** Rashes of various types, such as generalized maculopapular, lichenoid, urticarial, bullous lichen planus, psoriaform, and facial erythema; Peyronie's disease; reversible alopecia. ***Urinary System:*** Difficulty in micturition, including acute urinary bladder retention.

Following approval for marketing in the United Kingdom, a monitored release survey involving approximately 6,800 patients was conducted for further safety and efficacy evaluation of this product. Results of this survey indicate that the type, severity, and incidence of adverse effects were comparable to those cited above.

Potential Adverse Effects: In addition, other adverse effects not listed above have been reported with other beta-adrenergic blocking agents. ***Central Nervous System:*** Reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on psychometrics. ***Cardiovascular:*** Intensification of AV block (see CONTRAINDICATIONS). ***Allergic:*** Fever combined with aching and sore throat; laryngospasm, respiratory distress. ***Hematologic:*** Agranulocytosis, thrombocytopenic or nonthrombocytopenic purpura. ***Gastrointestinal:*** Mesenteric artery thrombosis, ischemic colitis. The oculomucocutaneous syndrome associated with the beta-blocker practolol has not been reported with labetalol HCl.

Clinical Laboratory Tests: There have been reversible increases of serum transaminases in 4% of patients treated with labetalol HCl and tested, and, more rarely, reversible increases in blood urea.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: DOSAGE MUST BE INDIVIDUALIZED. The recommended *initial* dosage is 100 mg *twice* daily whether used alone or added to a diuretic regimen. After two or three days, using standing blood pressure as an indicator, dosage may be titrated in increments of 100 mg bid every two or three days. The usual *maintenance* dosage of labetalol HCl is between 200 and 400 mg *twice* daily. Before use, see complete prescribing information for dosage details.

Glaxo Inc., Research Triangle Park, NC 27709 April 1988

CEFTIN® Tablets
(cefuroxime axetil)

BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in CEFTIN® Tablets product labeling.

CONTRAINDICATIONS: CEFTIN® is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH CEFTIN® IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO CEFTIN OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of

antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin in vitro.

Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: General: If an allergic reaction to CEFTIN® occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, eg, antihistamines, pressor amines, or corticosteroids.

As with other antibiotics, prolonged use of CEFTIN may result in overgrowth of nonsusceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution for individuals with a history of colitis.

Information for Patients: (Pediatric) CEFTIN is only available in tablet form. During clinical trials, the tablet was well tolerated by children who could swallow the tablet whole. Children who cannot swallow the tablet whole may have the tablet crushed and mixed with food (eg, applesauce, ice cream). However, it should be noted that the crushed tablet has a strong, persistent, bitter taste. Discontinuance of therapy due to the taste and/or problems of administering this drug occurred in 13% of children (range, 2% to 28% across centers). Thus, the physician and parent should ascertain, preferably while still in the physician's office, that the child can ingest CEFTIN reliably. If not, alternative therapy should be considered.

Interference with Laboratory Tests: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest® tablets), but not with enzyme-based tests for glycosuria (eg, Clinistix®, Tes-Tape®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving CEFTIN.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy: ***Pregnancy Category B:*** Reproduction studies have been performed in rats and mice at doses up to 50 to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime axetil. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since cefuroxime is excreted in human milk, consideration should be given to discontinuing nursing temporarily during treatment with CEFTIN.

ADVERSE REACTIONS: The adverse reactions to CEFTIN® are similar to reactions to other orally administered cephalosporins. CEFTIN was usually well tolerated in controlled clinical trials. Pediatric patients taking crushed tablets during clinical trials complained of the bitter taste of CEFTIN Tablets [see ADVERSE REACTIONS: Gastrointestinal and PRECAUTIONS: Information for Patients: (Pediatric)]. The majority of adverse events were mild, reversible in nature, and did not require discontinuance of the drug. The incidence of gastrointestinal adverse events increased with the higher recommended doses. Twenty-five (25) patients have received CEFTIN 500 mg twice a day for one to 2.5 months with no increase in frequency or severity of adverse events.

The following adverse reactions have been reported.

Gastrointestinal: Nausea occurred in 2.4% of patients. Vomiting occurred in 2.0% of patients. Diarrhea occurred in 3.5% of patients. Loose stools occurred in 1.3% of patients. There have been rare reports of pseudomembranous colitis.

Crushed tablets have a bitter taste. In pediatric clinical studies conducted with crushed tablets, complaints due to taste ranged from 0/8 (0%) in one center to 47/71 (66%) in another center.

Hypersensitivity: Rash (0.6% of patients), pruritus (0.3% of patients), and urticaria (0.2% of patients) have been observed. One case of severe bronchospasm has been reported among the approximately 1,600 patients treated with CEFTIN. Of the patients treated with CEFTIN who reported a history of delayed hypersensitivity to a penicillin and not a cephalosporin, 2.9% of patients experienced a delayed hypersensitivity reaction to CEFTIN.

Central Nervous System: Headache occurred in less than 0.7% of patients, and dizziness occurred in less than 0.2% of patients.

Other: Vaginitis occurred in 1.9% of female patients.

Clinical Laboratory Tests: Transient elevations in AST (SGOT, 2.0% of patients), ALT (SGPT, 1.6% of patients), and LDH (1.0% of patients) have been observed. Eosinophilia (1.1% of patients) and positive Coombs' test (0.4% of patients) have been reported.

In addition to the adverse reactions listed above that have been observed in patients treated with CEFTIN, the following adverse reactions and altered laboratory tests have been reported for cephalosporin class antibiotics:

Adverse Reactions: Allergic reactions including anaphylaxis, fever, colitis, renal dysfunction, toxic nephropathy, and hepatic dysfunction including cholestasis.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Altered Laboratory Tests: Increased prothrombin time, increased BUN, increased creatinine, false-positive test for urinary glucose, increased alkaline phosphatase, neutropenia, thrombocytopenia, and leukopenia.

Glaxo Inc., Research Triangle Park, NC 27709 February 1988

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1720s Founder Silvanus Bevan researched and reported on a revolutionary technique for smallpox inoculation.

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- Antihypertensive
  TRANDATE® (labetalol HCl) Tablets*
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*Please see Brief Summaries of Prescribing Information inside.

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Submitted by Student

From Chargaff E: *Voices in the Labyrinth.* New York, Seabury Press, 1977.

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"You can prove anything by statistics," is a common gibe. Its contrary is more nearly true—you can never prove anything by statistics. The statistician is dealing with the most complex cases of multiple causation. He may show the facts are in accordance with this hypothesis or that. But it is quite another thing to show all other possible hypotheses are excluded, and that the facts do not admit of any other interpretation than the particular one he may have in mind.

Submitted by Student

From Yule GU: *The Function of Scientific Method in Scientific Investigation.* Industrial Fatigue Research Board Report. 28. London, Her Majesty's Stationery Office, 1924, vol 28.

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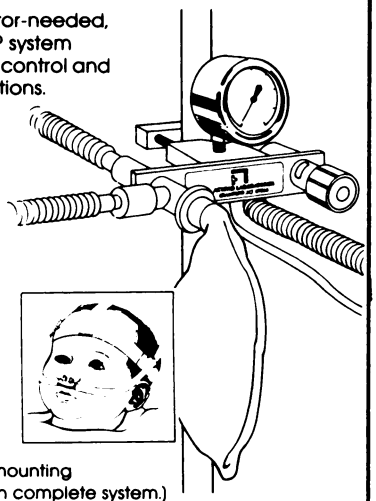

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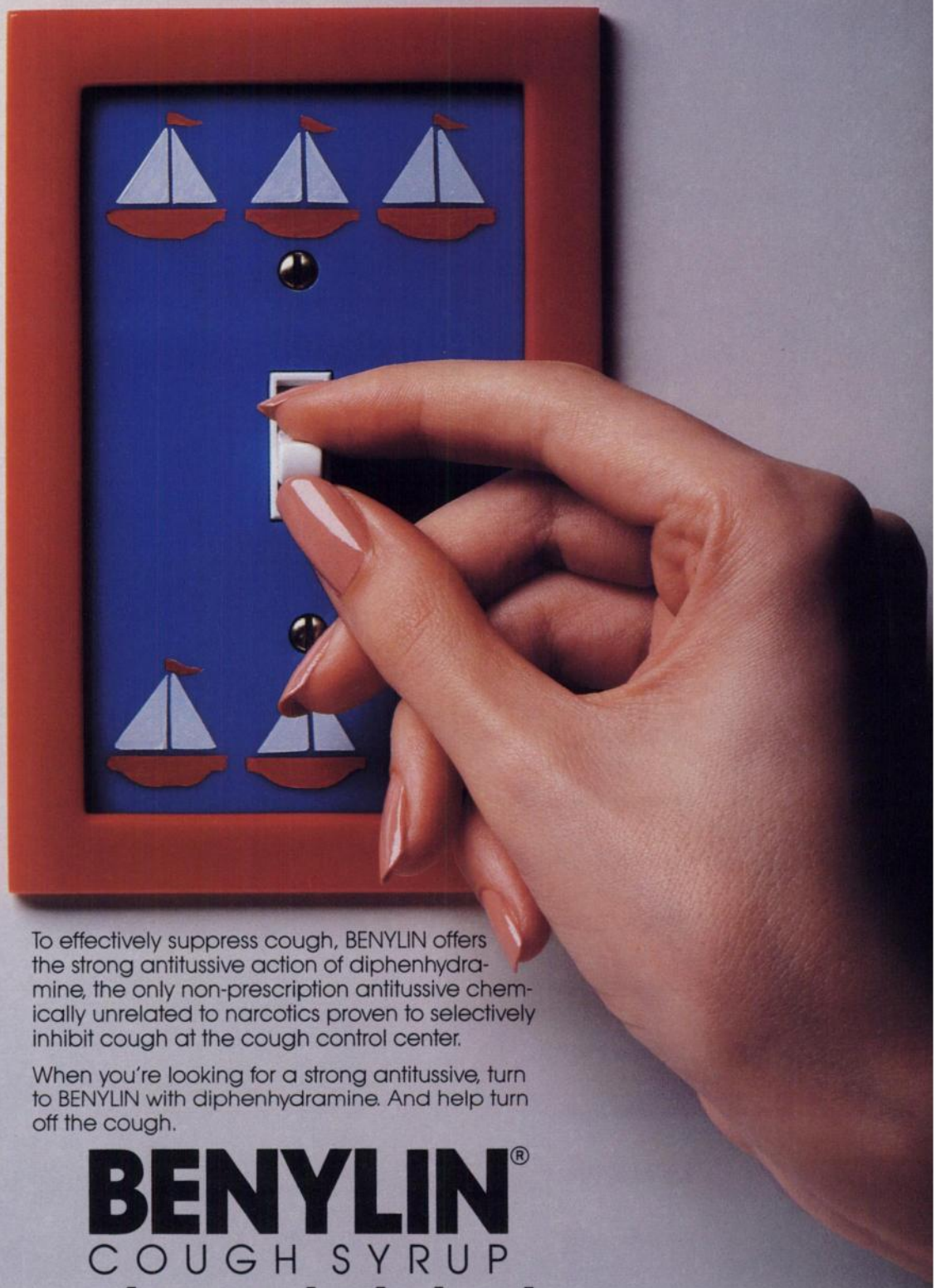

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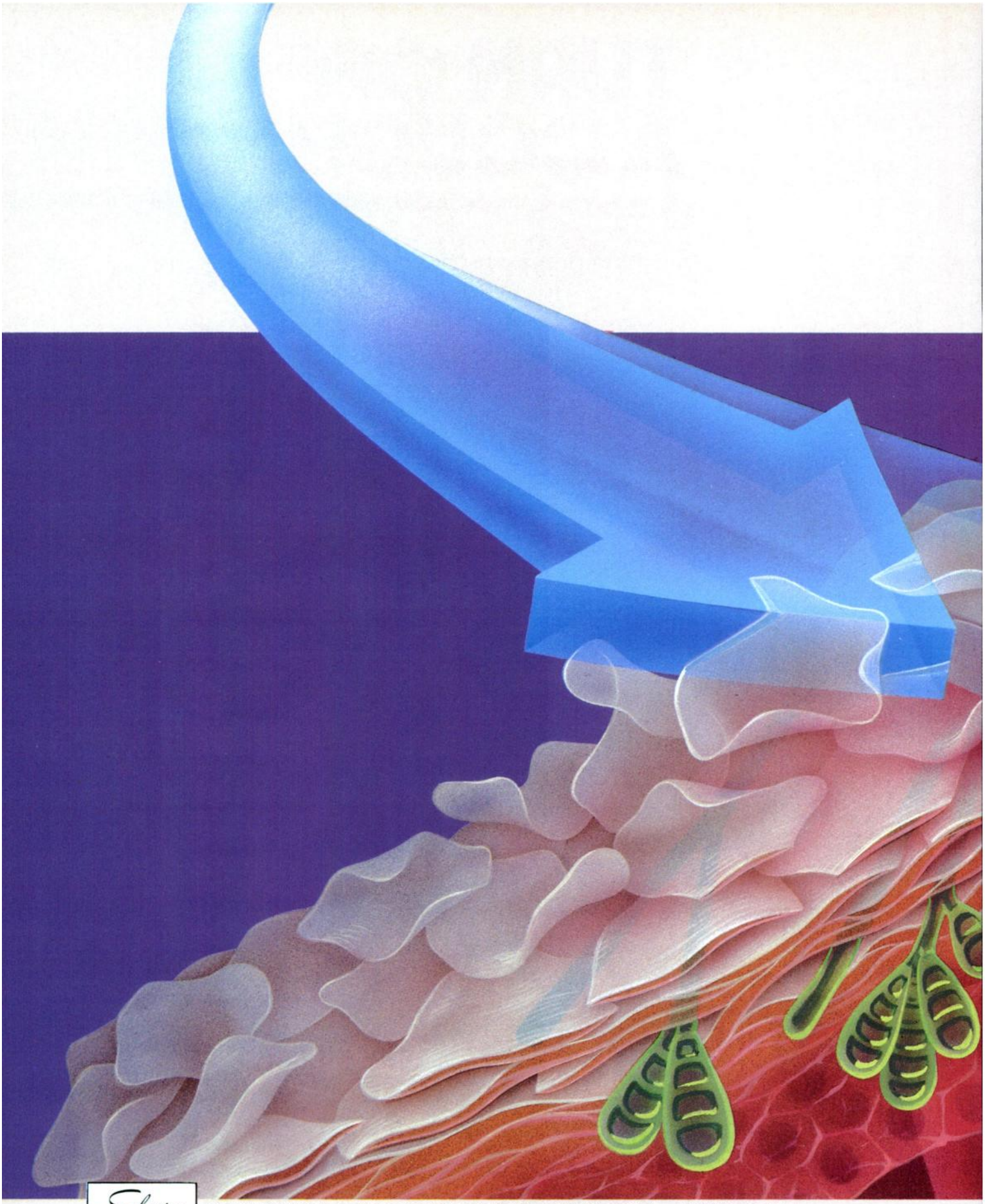

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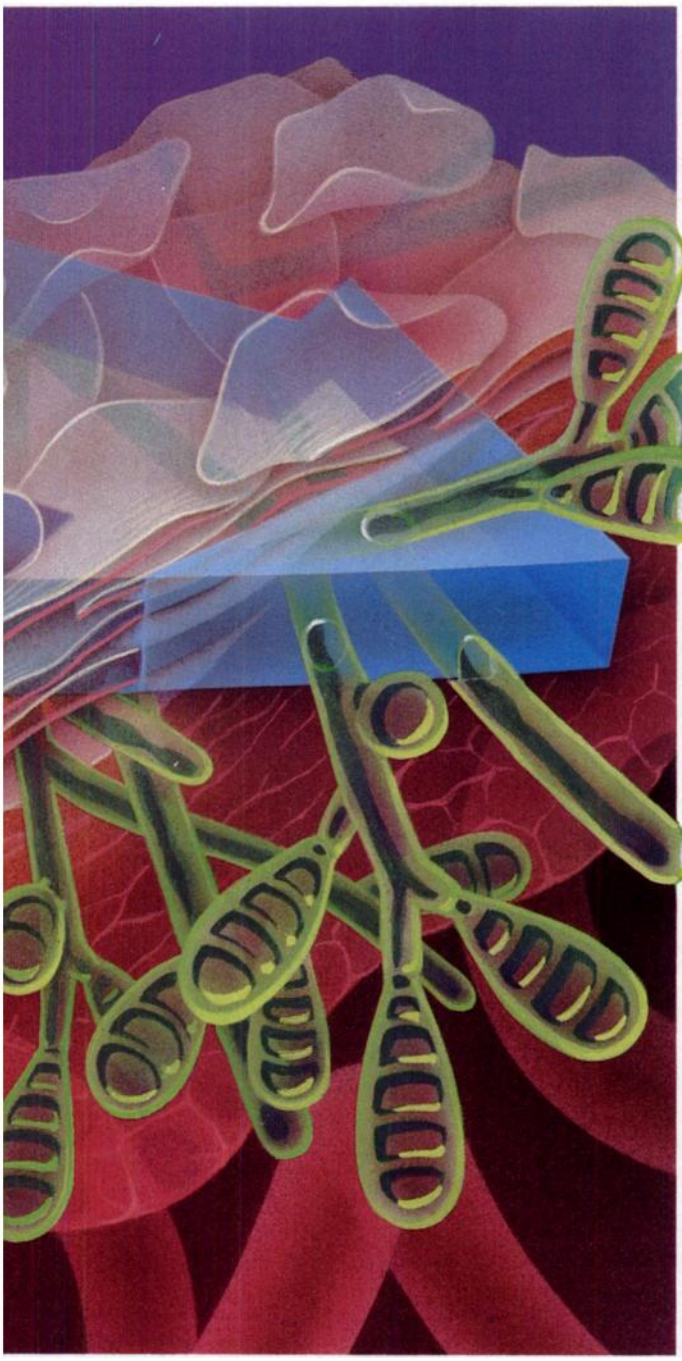
Artist's Representation

SPEEDS SYMPTOM RELIEF AS IT CURES* FUNGAL INFECTION.



Works on the surface and works on the source.

LOTRISONE quickly brings relief to irritating symptoms like redness, scaling and itching as it goes to work against invading dermatophytes. In clinical studies, this rapid response led to significantly more patients completing their course of therapy with LOTRISONE than with clotrimazole — resulting in greater treatment success.

Low incidence of adverse reactions.

In safety evaluations of 200 patients, only 6 had any adverse experience — usually mild. There were no reports of skin thinning or telangiectasia.

DUAL-ACTION

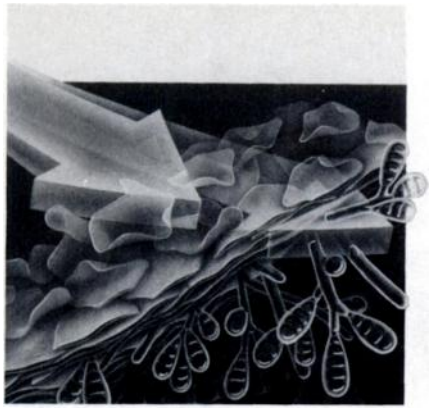
LOTRISONE®

brand of clotrimazole, USP and betamethasone dipropionate, USP CREAM

THE LOGICAL FIRST CHOICE FOR FUNGAL INFECTION.

Please see next page for brief summary of prescribing information.

**A mycologic cure consists of negative culture at the end of treatment and two weeks post-treatment.*



DUAL-ACTION LOTRISONE®

brand of clotrimazole, USP and betamethasone dipropionate, USP CREAM

SPEEDS SYMPTOM RELIEF AS IT CURES* FUNGAL INFECTION.

For Dermatologic Use Only—
Not for Ophthalmic Use

DESCRIPTION *Each gram of LOTRISONE Cream contains 10.0 mg clotrimazole, USP, and 0.64 mg betamethasone dipropionate, USP (equivalent to 0.5 mg betamethasone), in a hydrophilic emollient cream consisting of purified water, mineral oil, white petrolatum, cetearyl alcohol, ceteareth-30, propylene glycol, sodium phosphate monobasic, and phosphoric acid; benzyl alcohol as preservative.*

LOTRISONE is a smooth, uniform, white to off-white cream.

INDICATIONS AND USAGE *LOTRISONE Cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis.*

CONTRAINDICATIONS *LOTRISONE Cream is contraindicated in patients who are sensitive to clotrimazole, betamethasone dipropionate, other corticosteroids or imidazoles, or to any ingredient in this preparation.*

PRECAUTIONS ***General*** *Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.*

*Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings. (See **DOSAGE AND ADMINISTRATION** section.)*

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.

*Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. (See **PRECAUTIONS-Pediatric Use**.)*

If irritation or hypersensitivity develops with the use of LOTRISONE Cream, treatment should be discontinued and appropriate therapy instituted.

Information for Patients *Patients using LOTRISONE Cream should receive the following information and instructions:*

1. *This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.*
2. *The medication is to be used for the full prescribed treatment time, even though the symptoms may have improved. Notify the physician if there is no improvement after one week of treatment for tinea cruris or tinea corporis, or after two weeks for tinea pedis.*
3. *Patients should be advised not to use this medication for any disorder other than for which it was prescribed.*
4. *The treated skin areas should not be bandaged or otherwise covered or wrapped as to be occluded. (See **DOSAGE AND ADMINISTRATION** section.)*
5. *When using this medication in the groin area, patients should be advised to use the medication for two weeks only, and to apply the cream sparingly. The physician should be notified if the condition persists after two weeks. Patients should also be advised to wear loose fitting clothing. (See **DOSAGE AND ADMINISTRATION** section.)*
6. *Patients should report any signs of local adverse reactions.*
7. *Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressing. (See **DOSAGE AND ADMINISTRATION** section.)*
8. *Patients should avoid sources of infection or reinfection.*

Laboratory Tests *If there is a lack of response to LOTRISONE Cream, appropriate microbiological studies should be repeated to confirm the diagnosis and rule out other pathogens before instituting another course of antimycotic therapy.*

The following tests may be helpful in evaluating HPA axis suppression due to the corticosteroid component:

Urinary free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, Impairment of Fertility *There are no animal or laboratory studies with the combination clotrimazole and betamethasone dipropionate to evaluate carcinogenesis, mutagenesis or impairment of fertility.*

An 18-month oral dosing study with clotrimazole in rats has not revealed any carcinogenic effect.

In tests for mutagenesis, chromosomes of the spermatophores of Chinese hamsters which had been exposed to clotrimazole were examined for structural changes during the metaphase. Prior to testing, the hamsters had received five oral clotrimazole doses of 100 mg/kg body weight. The results of this study showed that clotrimazole had no mutagenic effect.

Pregnancy Category C *There have been no teratogenic studies performed with the combination clotrimazole and betamethasone dipropionate.*

Studies in pregnant rats with intravaginal doses up to 100 mg/kg have revealed no evidence of harm to the fetus due to clotrimazole.

High oral doses of clotrimazole in rats and mice ranging from 50 to 120 mg/kg resulted in embryotoxicity (possibly secondary to maternal toxicity), impairment of mating, decreased litter size and number of viable young and decreased pup survival to weaning. However, clotrimazole was not teratogenic in mice, rabbits and rats at oral doses up to 200, 180 and 100 mg/kg, respectively. Oral absorption in the rat amounts to approximately 90% of the administered dose.

Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.

There are no adequate and well-controlled studies in pregnant women on teratogenic effects from a topically applied combination of clotrimazole and betamethasone dipropionate. Therefore, LOTRISONE Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Drugs containing corticosteroids should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers *It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk caution should be exercised when LOTRISONE Cream is used by a nursing woman.*

Pediatric Use *Safety and effectiveness in children below the age of 12 have not been established with LOTRISONE Cream. However, dosage forms containing concentrations of clotrimazole and of betamethasone dipropionate found in LOTRISONE Cream have been demonstrated to be safe and effective when used as indicated and in the recommended dosages.*

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical dermatologics containing a corticosteroid to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS *The following adverse reactions have been reported in connection with the use of LOTRISONE Cream: paresthesia in 5 of 270 patients, maculopapular rash, edema, and secondary infection, each in 1 of 270 patients.*

Adverse reactions reported with the use of clotrimazole are as follows: erythema, stinging, blistering, peeling, edema, pruritus, urticaria, and general irritation of the skin.

The following local adverse reactions are reported infrequently when topical corticosteroids are used as recommended. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria.

OVERDOSAGE *Acute overdosage with topical application of LOTRISONE Cream is unlikely and would not be expected to lead to a life-threatening situation.*

*Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. (See **PRECAUTIONS**.)*

HOW SUPPLIED *LOTRISONE Cream is supplied in 15-gram (NDC 0085-0924-01), and 45-gram tubes (NDC 0085-0924-02); boxes of one.*

Store between 2° and 30°C (36° and 86°F).

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LS-A065/13630100

**A mycologic cure consists of negative culture at the end of treatment and two weeks post-treatment.*

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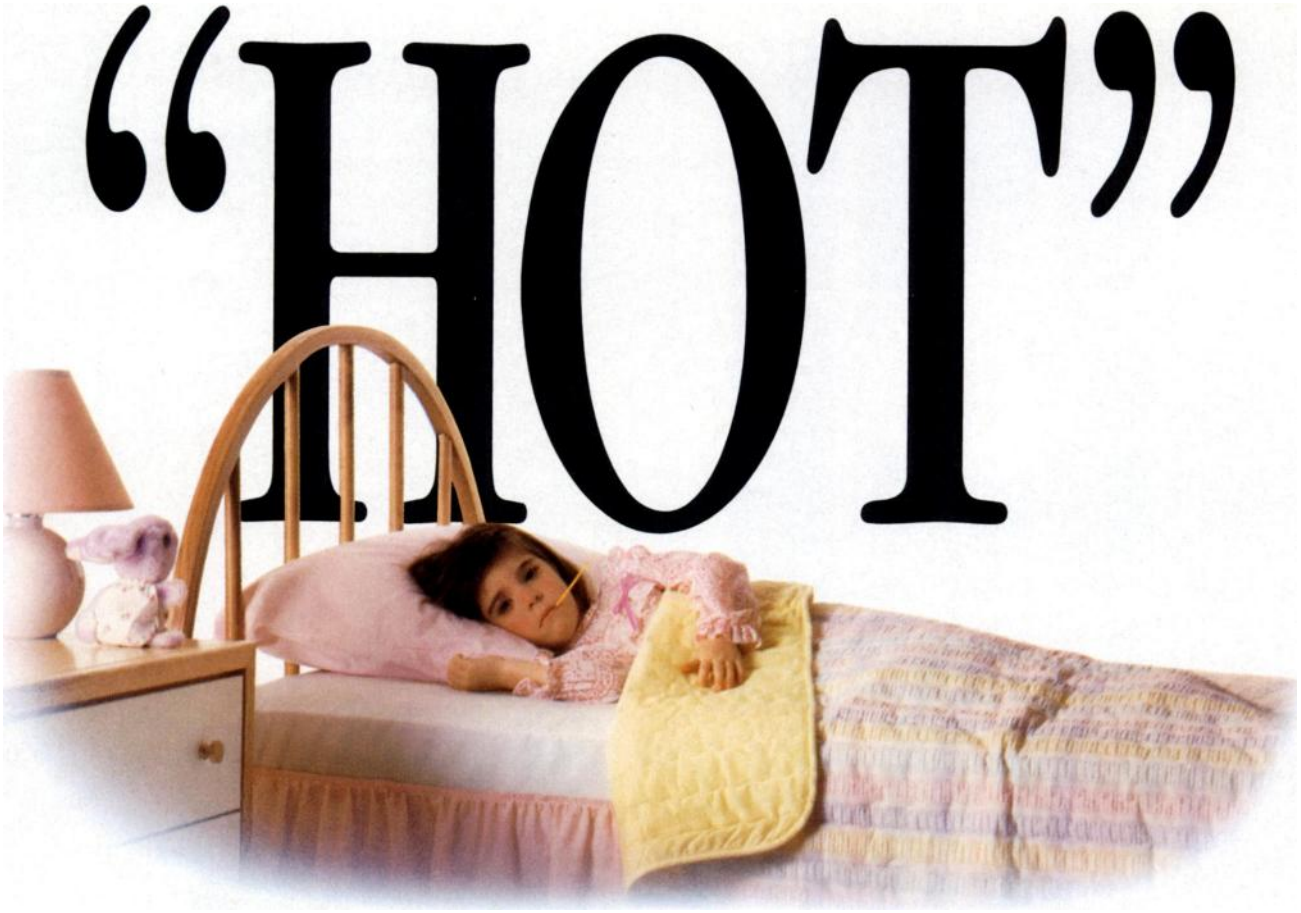

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- ☐ Easy-to-swallow 160 mg Junior Strength Coated Caplets for 6- to 14-year-olds

Remember, TYLENOL® is clinically proven as effective an antipyretic as aspirin, with a superior safety profile.[1,2] And parents can easily find your recommendation, because TYLENOL® products are more widely available in food and drug stores than any other brand.[3] So next time a little patient is "Hot!" with fever, make your first choice TYLENOL® acetaminophen.

References: 1. Tarlin L, et al: *Am J Dis Child* 1972;124:880-882. 2. Aspirin or paracetamol? *Lancet* 1981;II:287-289. 3. Data on file, McNeil Consumer Products Company.

Children's and Junior Strength

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