Today's hypertensives with new concerns...

THE CARDURA GENERATION

Choose CARDURA: first-line therapy for a new generation of hypertensives.

Choose CARDURA for around-the-clock blood pressure control that doesn’t jeopardize blood lipids or blood sugar.¹³

CARDURA is well tolerated. In placebo-controlled studies, only three common side effects were reported significantly more often than with placebo: dizziness, somnolence, and fatigue. These were generally mild and transient. Only 2% of patients discontinued therapy due to adverse effects—the same as with placebo. Syncope has been reported, but rarely (<1%).

ONCE-A-DAY CARDURA®
(doxazosin mesylate) Scored Tablets 1 mg, 2 mg, 4 mg, 8 mg

HYPERTENSION CONTROL FOR A NEW GENERATION.
CARBAMATE (doxazosin mesylate) Tablets

Brief Summary of Prescribing Information

INDICATIONS AND USAGE
CARBUDICA™ (doxazosin mesylate) is indicated for the treatment of hypertension.

The active ingredient in CARBUDICA™ is doxazosin mesylate in combination with ramipril.

CONTRAINDICATIONS
CARBUDICA™ is contraindicated in patients with a known sensitivity to quinazolines (e.g., prazosin, terazosin).

WARNING
Sympotom and “First-dose” Effect:
Doxazosin-like, especially alpha-1-adrenergic blocking agents, can cause marked hypotension, especially in the supine position, with syncope and other orthostatic reactions.

ADVERSE REACTIONS
The most common adverse reactions associated with CARBUDICA™ therapy are lower blood pressure, dizziness, and headache.

Carcinogenicity in Animals:
An increased incidence of myeloid leukemia or fibrosarcoma was observed in the Sprague-Dawley rat strains after 6 decades of dietary administration of concentrations calculated to provide 20 mg/kg/day for 26 weeks and 90 mg/kg/day and after 12 months of dietary administration of concentrations calculated to provide 40 mg/kg/day (4612 life-years) and after 12 months of dietary administration of concentrations calculated to provide 60 mg/kg/day (168 life-years).

MYOCARDIAL INFLAMMATION:
Myocardial inflammation was observed in both rats and mice treated in the same manner as CARBUDICA™ treatment. The incidence of myocardial inflammation was observed at lower doses (10 mg/kg or 20 mg/kg or 50 mg/kg) and at 20 mg/kg and 100 mg/kg, respectively.

GASTROintestinal:
There is no evidence that suggests that CARBUDICA™ is associated with an increased risk of gastrointestinal symptoms.

Gastrointestinal:
There are no significant differences in incidence of side effects, except for dizziness (indicating postural hypotension), in the trials conducted with CARBUDICA™. Postural reactions and edema appear to be dose-related.

Skin Adverse Reactions:
- Rash
- Pruritus
- Urticaria

MUSCULOSKELETAL:
- Arthralgia
- Arthritis
- Myalgia
- Muscular weakness

CENTRAL And PERIPHERAL N.S.:
- Headache
- Dizziness
- Inability to urinate

Drug/Laboratory Interactions:
- None known.
1000 mg of Extra Strength Tylenol® is as effective as 400 mg of ibuprofen for mild-to-moderate pain. Compared to aspirin, Extra Strength Tylenol® is 26% more effective (SPID) than 650 mg of aspirin. For osteoarthritis, it effectively manages the noninflammatory.

Pure analgesia that works
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TAGAMET®, (Brand of cimetidine)
See complete prescribing information in SmithKline Beecham Pharmaceuticals literature or PDR. The following is a brief summary.
Indications and Usage: 1. Short-term treatment of active duodenal ulcer: (a) maintenance therapy following successful ulcer healing by medical therapy; (b) maintenance therapy following ulcer recurrence after initial ulcer healing by medical therapy; (c) maintenance therapy following ulcer recurrence after initial ulcer healing by medical therapy. (d) maintenance of healing of active benign gastric ulcer; (e) control of gastroesophageal reflux disease; (f) prevention of upper gastrointestinal bleeding in elderly patients; (g) treatment of pathological hypersecretory conditions.
Contraindications: Tagamet is contraindicated for patients known to have hypersensitivity to the product.
Precautions: Rare instances of skin anaphylactoid reaction and hyperkalemia have been reported following the rapid administration of Tagamet (cimetidine hydrochloride) injection by intravenous route.
Symptomatic response to Tagamet therapy does not preclude the presence of a gastric malignancy. There have been rare reports of transient healing of gastric ulcers despite incomplete documentation of malignancy.
Reducible collagenous stomach has been observed on occasion, predominantly in severely ill patients. Tagamet has been reported to reduce the incidence of resolution of wall-sided antral polyps, hyperpigmentation, nodularity, edematous, linitis plastica, and necrotic ulceration. Close monitoring of polypoid tissue is recommended, and judicious use of the antral polypoid dose may be necessary when Tagamet is administered concurrently. Intervention with phenolization, lipectomy and thyroepinephryonectomy has also been reported to produce abatement of clinical symptoms.
However, a cross-over study in healthy subjects receiving either tagamet 300 mg every 6 hours or placebo concurrently with a 400 mg dose of theophylline (Theo-Dur®), Key Pharmaceuticals Inc., administered less frequently in a steady-state equivalent peak plasma level with 300 mg every 6 hours, particularly in subjects aged 54 to 70 years and debarred. Data beyond these data are not available. (Note: All patients receiving theophylline should be monitored appropriately, regardless of concurrent drug therapy.)
In a 24-month toxicity study in rats, at dose levels in rats, it was noted that the median dosage of tagamet and the human equivalent, orally administered, would result in the median dosage in the rat in humans. A weak antitoxic effect has been demonstrated in animals. In human subjects, Tagamet has been shown to produce no effect on spermatogenesis, sperm count, motility, morphology or in vitro fertilizing capacity.
Fertility Category: B. Reproduction studies have been performed in mice and rats at doses up to 2 times the maximum human dose administered and have revealed no evidence of impaired fertility or harm to the fetus due to Tagamet. 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.

How Supplied: Tablets: 200 mg tablets in bottles of 100, 300 mg tablets in bottles of 100 and Single Unit Packages of 100 (intended for institutional use only). 400 mg tablets in bottles of 100 and Single Unit Packages of 100 (intended for institutional use only).
Injection: 300 mg/mL in 30 mL and 40 mL vials, in 5 mL and 10 mL multidose vials in packages of 10 (intended for institutional use only).
PAIN

RELIEF
Put out the fire fast with Tagamet®

Over 80% of duodenal ulcer patients reported relief of nighttime pain after only one dose of Tagamet 800 mg Tiltab Tablets h.s.¹
And Tagamet 800 mg b.i.d. provides prompt, continuing heartburn relief, even in severe, erosive esophagitis.²

Before prescribing, please see brief summary of prescribing information on adjacent page.
Living In Medicine

Gained in Translation
Michael D. Anderson, MD

Special Articles

American Medical Association
Diagnostic and Treatment Guidelines on Domestic Violence

Practice Commentary
Jane T. Carswell, MD

Somatic Consequences of Violence Against Women
Mary P. Koss, PhD, Lynette Heslet, RN, BS

‘The Hidden Epidemic’: Physician Leadership Is Essential
Antonia C. Novello, MD, MPH, US Surgeon General

Original Contributions

Clinical Competence of Family Physicians: The Patient Perspective
Arch G. Mainous III, PhD, Alan K. David, MD

Patients’ Knowledge About Fats and Cholesterol in the Community
Cholesterol Survey Project
Robert B. Kelly, MD, MS; Judith A. Hazey; Shelly H. McMahon, RD

Practice Commentary
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ENGINEERED FOR THE CONTROL YOU WANT, THE PROTECTION THEY NEED.

IN HYPERTENSION SHIFT TO

ONCE-A-DAY VERELAN®
Verapamil HCl 120 mg
180 mg
240 mg
PELLET-FILLED CAPSULES

PROTECTS your hypertensive patients for 24 hours¹

REDUCES wide variations in BP control²

NEGLIGIBLE discontinuation due to side effects¹

DOSED once daily at all doses

Wyeth-Ayerst Laboratories, a division of American Cyanamid Company
Wayne, New Jersey 07470

Constipation, which can easily be managed in most patients, is the most frequently reported side effect of verapamil.

Please see brief summary of Prescribing Information including CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS on adjacent page.
VERELAN® shock, blocking
Several severe patients with verapamil
Editorial Assistant
capsule.
CHF
ventricular and
of the heart
Block-total accessory pathway (see WARNINGS).
Carr
Verapamil
AA,
ventricular block.
and/or ventricular fibrillation has been reported in patients with atrial fibrillation. A coexisting accessory AV pathway may be a factor in some cases (see WARNINGS).

WILLIAMS
others. Several cases of hypothalamic injury have been demonstrated to be caused by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial fibrillation and an accessory AV pathway (e.g., WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving IV verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (second- or third-degree, 0.8%). Development of marked first-degree block or progression to second- or third-degree block requires reduction in dosage or, rarely, discontinue and institution of appropriate therapy. Sinus bradycardia, second-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypotrophic cardiomyopathy who were treated with verapamil.

PRECAUTIONS
Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 20% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdose. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular and blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of exacerbation of angina and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol clearance may occur with combined use. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extraluminal clearance of digoxin. The digoxin dose should be reduced when verapamil is given and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Discopyramide should not be given within 48 hours before or after verapamil administration. Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Verapamil has been given concomitantly with short- and long-acting nitrites without any undesirable drug interactions. Interaction between cimetidine and chronically administered verapamil has not been studied. In healthy volunteers, clearance and the half-life of verapamil was reduced or unchanged. Concomitant use of lithium and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully.

Verapamil may increase carbenicillin concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenothiazine may increase verapamil clearance. Verapamil may increase serum levels of cyclosporine. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (nuraxne and depolarizing); dosage reduction may be required. Adequate animal carcinogenicity studies have not been performed. One study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use. Safety and efficacy of verapamil in children below the age of 18 years have not been established.

ADVERSE REACTIONS
Reversible (upon discontinuation of verapamil) nonproductive, paralytic ileus has been infrequently reported in association with the use of verapamil. In clinical trials with 233 hypertensive patients on VERELAN for more than 1 week, the following adverse reactions were reported: constipation (7.4%); headache (5.3%); dizziness (4.2%); diarrhea (3.2%); dyspepsia (2.5%); rash (1.4%); ankle edema (1.4%); sleep disturbance (1.4%); myalgia (1.1%); in clinical trials of other formulations of verapamil HCl (N = 4,954), the following reactions have occurred at rates greater than 1%: constipation (7.3%); dizziness (3.3%); nausea (2.7%); dyspepsia (2.5%); edema (1.9%); headache (2.2%); rash (1.3%); CHF/pulmonary edema (1.8%); fatigue (1.7%); bradycardia (HR 50-55/min) (1.4%); AV block-total 1°, 2° (1.2%); 2° and 3° (0.8%); flushing (0.5%); elevated liver enzymes (see WARNINGS). The following reactions, reported in 1% or less of patients, occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain. Cardiovascular: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope. Disguise System: anemia, oral or dry mouth, gastrointestinal distress, gingival hyperplasia, Hemic and Lymphatic: ecchymosis or bruising. Nervous System: carbovascular accident, confusion, equilibrium disorder, depression, dizziness, headache, insomnia, myoclonus, neurotic disturbances, numbness, paresthesia, syncope, tremor. Skin: rash, pruritus, other skin reactions, exfoliative dermatitis, hyperpigmentation, hyperkeratosis, itching, localized maculopapular rash, Stevens-Johnson syndrome, vesiculobullous rash. Special Senses: blurred vision, Urogenital: gynecomastia, impotence, increased urination, scanty menstruation.


Brief Summary
VERELAN®
Verapamil HCl
Sustained-Release Pellet-Filled Capsules

For complete Prescribing Information, consult package insert.

CLINICAL PHARMACOLOGY
Food does not affect the extent or rate of the absorption of verapamil from the controlled release VERELAN capsule.

Atrioventricular block can occur in patients without preexisting conduction defects (see WARNINGS). Acceleration of ventricular rate and/or ventricular fibrillation has been reported in patients with atrial fibrillation or atrial flutter and a coexisting accessory AV pathway following administration of verapamil (see WARNINGS). In patients with hepatic insufficiency, metabolism is delayed and elimination half-life prolonged up to 14 to 16 hours (see PRECAUTIONS). The volume of distribution is increased, and plasma clearance reduced to about 30% of normal.

CONTRAINDICATIONS
Severe LV dysfunction (see WARNINGS). Hypotension (cystolic pressure < 90 mmHg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), second- or third-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (e.g., WPW or LGL syndromes), (see WARNINGS), hypersensitivity to verapamil.

WARNINGS
Verapamil should be avoided in patients with severe LV dysfunction (e.g., ejection fraction < 30%) or moderate-to-severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta blocker. Control mild heart failure with optimal digitalization and/or diuretics before VERELAN is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported.

...
There's a method to our mildness

A method no soap can claim
Dove® is special. It has a unique, non-soap surfactant that replaces soap's alkaline end group with a milder isethionyl radical. This results in a non-soap, pH-neutral formulation that also contains 1/4 moisturizing cream.

A mildness no soap can touch
Dove Bar’s unique, non-soap formula is milder to skin than any soap. Clinical trials prove it. Dove Bar causes significantly less irritation and dryness — and helps the skin retain needed moisture.

The result: Dove leaves skin softer and smoother than skin washed with soap. So recommend Dove—for mildness no soap can touch.

Beauty Bar and Beauty Wash Available in original and Unscented
Membrane-controlled NICODERM® Assures

Membrane-controlled Means That Nicotine Delivery Is Less Dependent on Skin Permeability.

Unique Rate-controlling Membrane
The only nicotine transdermal system that is membrane-controlled—not skin-controlled—resulting in 24-hour nicotine plasma levels that help suppress physiologic withdrawal symptoms.

1. Nicotine in the adhesive layer provides rapid delivery of nicotine during the initial few hours.
2. Nicotine delivery from the drug reservoir thereafter depends on the rate-controlling membrane with less dependence on skin permeability. It then passes through the adhesive layer and reaches the systemic circulation via the capillaries.

Artist's interpretation of the layers of the NICODERM transdermal system.

© 1992, Marion Merrell Dow Inc. NIDA027/A7022 6802M2
Reproducible Delivery of Nicotine

10-Week Weaning Program. Convenient “6-2-2” Schedule for Nicotine Elimination and Committed Quitter’s Program as an Aid to a Comprehensive Behavioral Smoking-cessation Program.

- Clinical study demonstrates safety in stable coronary artery disease patients* (Start with 14 mg/day)
- Smallest dimensions of any nicotine patch available. Superthin profile avoids catching on clothes
- 2-week packaging. Convenient for your patients to initiate treatment

The product should be used as part of a comprehensive behavioral smoking-cessation program. The use of NICODERM beyond 3 months has not been studied.

The specific effects of NICODERM on fetal development are unknown. Therefore, pregnant or nursing smokers should be encouraged to attempt cessation using educational and behavioral interventions before using pharmacological approaches. Marion Merrell Dow does not recommend use of NICODERM in pregnant women.

The risks of nicotine replacement in patients with certain cardiovascular and peripheral vascular diseases should be weighed against the benefits of including nicotine replacement in a smoking-cessation program for them.

Dosage adjustment of concomitant medications may be necessary. (See drug interactions.)

Please see brief summary of prescribing information on an adjacent page.

* As seen in an 8-week study. NICODERM should be used with caution, if at all, in patients during the immediate postmyocardial infarction period, in patients with life-threatening arrhythmias, and in patients with severe or worsening angina pectoris. (See Precautions.)
NICODERM®

(intact)
INTRODUCING NEW Ismo™ 20 mg tablets (isosorbide mononitrate)
A NEW NITRATE FOR ANGINA PREVENTION

Predictable pharmacokinetics

Effective and well tolerated

Unique dosing regimen avoids tolerance and rebound

To maintain antianginal efficacy and to avoid tolerance and rebound, the recommended dosing schedule of 20 mg, twice daily, given 7 hours apart (with a 17-hour dose-free interval), must be followed carefully.

* I smo is not recommended for use in aborting acute anginal episodes. As with other long-acting nitrates, I smo is not recommended in patients with acute myocardial infarction (MI) or congestive heart failure (CHF). Paradoxical bradycardia and increased angina pectoris may accompany I smo-induced hypotension. Long-acting nitrates may aggravate angina caused by hypertrophic cardiomyopathy. The most common side effect, headache, may be resolved with mild analgesics.

*There are no data that suggest this dose-free interval is appropriate with any other long-acting nitrate.

*The dose-free interval sufficient to avoid tolerance to isosorbide mononitrate is not completely defined.

NEW I smo (isosorbide mononitrate)

Please see brief summary of prescribing information on adjacent page.
**Ismo**
(isosorbide mononitrate) 20 mg tablets

**BRIEF SUMMARY (FOR FUL UPPR INFORMATION, SEE PACKAGE INSERT)**

**Indications and Usage** Ismo is indicated for prevention of angina pectoris due to coronary artery disease. The onset of action is not rapid enough for it to be useful in aborting an acute anginal episode.

**Clinical Pharmacology** Isosorbide mononitrate is the major active metabolite of isosorbide dinitrate. Most of the clinical activity of the dinitrate comes from the mononitrate. Ismo is not subject to first-pass metabolism in the liver and the absolute bioavailability of isosorbide mononitrate from ismo tablets is nearly 100%. The rate of clearance of ismo is the same in healthy young adults, in patients with various degrees of renal, hepatic, or cardiac dysfunction, and in the elderly.

Several well-controlled studies have demonstrated that active nitrates are indistinguishable from placebo after 24 hours (or less) of continuous therapy due to the development of tolerance. Only after nitrates are absent from the body for several hours is their antianginal efficacy restored. The drug-free interval sufficient to avoid tolerance to isosorbide mononitrate is not completely defined. The only regimen shown to avoid development of tolerance with isosorbide mononitrate involves daily doses of ismo twice a day. Ismo alone given 7 hours apart, or ismo and nitrates given for 12 hours between the second dose of each day and the first dose of the next day. Taking account of the relatively long half-life of isosorbide mononitrate this result is consistent with those obtained for other organic nitrates.

The same twice-daily regimen of ismo tablets successfully avoided significant rebound/withdrawal effects. In studies of other nitrates, the incidence and magnitude of such phenomena appear to be highly dependent upon the schedule of nitrate administration.

**Contraindications** Allergic reactions are extremely rare, but do occur. Ismo is contraindicated in patients with:**

- **Warnings** Because the effects of ismo are difficult to terminate rapidly and have not been established in patients with acute myocardial infarction (MI) or congestive heart failure (CHF), this drug is not recommended in these patients. If ismo is used in these patients, careful clinical or hemodynamic monitoring is required to avoid the hazards of hypotension and tachycardia.

- **Precautions** General: Severe hypotension, in particular with upright posture, may occur even with small doses. Therefore, use with caution in patients who may be volume depleted or who are already hypotensive. Paradoxical bradycardia and increased pulse pressure may accompany ismo-induced hypotension.

- **Nitrites** may aggravate angina caused by a hyperemic cardiomyopathy.

**INFORMATION FOR PATIENTS** Tell patients they must carefully follow the prescribed dosing schedule (2 doses taken 7 hours apart) to maintain the antianginal effect (eg, take first dose on awakening and second dose 7 hours later).

Daily headaches sometimes accompany treatment with nitrates, including ismo, and are a marker of drug activity. Patients with headaches should not alter their treatment schedule since loss of headache may be associated with simultaneous loss of antianginal efficacy. Headaches may be treated with aspirin and/or acetaminophen without affecting the antianginal activity of ismo.

Light-headedness, especially just after rising from a recumbent or seated position, may occur. This may be more frequent in patients who have consumed alcohol.

**Drug Interactions** Vasodilating effects of ismo may be additive with those of other vasodilators, especially alcohol.

Marked symptomatic orthostatic hypotension has been reported when calcium channel blockers and organic nitrates were used in combination. Dose adjustments of either class of agents may be necessary.

**Carcinogenesis, Mutagenesis, and Impairment of Fertility** No carcinogenic effects were observed in mice or rats exposed to ismo, nor were adverse effects on fertility observed.

**Obstetric Use** There have been no controlled studies in pregnant women. Use during pregnancy only if potential benefit justifies potential fetal risk.

**NURSING MOTHERS** Excretion in human milk is unknown. Use caution if administered to a nursing woman.

**Pediatric Use** Safety and effectiveness have not been established.

**Adverse Reactions** Frequency of Adverse Reactions in Patients Receiving Ismo Twice a Day (Dose Overdose).

**Overdosage** The ill effects of overdosage are generally related to the ability of ismo to induce vasodilation, venous pooling, reduced cardiac output and hypotension. Symptoms include increased intracranial pressure, with or without all of persistent throbbing headache, confusion, and moderate fever; vertigo; palpitations; visual disturbances; nausea and vomiting (possibly with colic and even bloody diarrhea); syncope (especially with upright posture); air hunger and dyspnea; later followed by reduced respiratory effort; diaphoresis; with the skin either flushed or cold and clammy; heart block and bradycardia; paralytic coma; seizures; and death.

Serum levels have no role in managing overdose. The likely lethal dose in humans is unknown.

There is neither a specific antidote to ismo overdose, nor data to suggest a means for accelerating its elimination from the body. dialysis is ineffective. Hypotension associated with ismo overdose results from venodilatation and arterial hypotension, therefore, direct therapy toward an increase in central fluid volume. Use of arterial vasocorticosteroids (eg, epinephrine) is likely to do more harm than good. In patients with renal failure or CHF, treatment of ismo overdose may be difficult and require invasive monitoring.

Methemoglobinemia has occurred in patients receiving other organic nitrates, and probably could occur as a side effect of ismo. There are case reports of significant methemoglobinemia in association with moderate overdose of organic nitrates. None of these affected patients had been thought to be unusually susceptible. Suspect the diagnosis in patients who exhibit signs of impaired oxygen delivery despite adequate cardiac output and a normal arterial pH. Classically, methemoglobinemia studied in blood is a cherry brown, without color change on exposure to air. The treatment of choice for methemoglobinemia is metyrapone and 1-2 mg intravenous pyridine.

**Dosage and Administration** The recommended regimen of ismo tablets is 20 mg (one tablet) twice daily, with the two doses given 7 hours apart. For most patients, this can be accomplished by taking the first dose on rising and the second dose 7 hours later. This dosing regimen provides a daily nitrate-free interval to avoid development of refractory tolerance (see Clinical Pharmacology).

Well-controlled studies have shown that tolerance to ismo tablets is avoided when the twice daily regimen in which the two doses are given 7 hours apart is used. This regimen has been shown to produce a drug free interval of 1 hour after the first dose and lasting at least 5 hours after the second dose. The duration of action of a single oral dose is not known. In several studies, large controlled studies with other nitrates suggest that no dosing regimen should be expected to provide more than 12 hours of continuous antianginal efficacy per day.

Dose adjustments are not necessary in the elderly patients or in patients with altered renal or hepatic function.

This Brief Summary is based upon the current Ismo direction circular, CI 427-1, Issued January 10, 1992.

**AH ROBINS**

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**CHOOSE YOUR WEAPON**

Crunch a carrot. Snack on strawberries. In the fight to eliminate cancer, some of the best kept secret weapons are right behind your refrigerator door. Look for foods low in fat, high in fiber, and rich in Vitamins A and C. Choosing your weapon is a matter of habit. Fruit instead of fat. Mustard instead of mayo on that midnight sandwich. For a more comprehensive list, call the American Cancer Society at 1-800-ACS-2345, and turn your refrigerator into an arsenal of great tasting weapons.

**There's nothing mightier than the sword.**
Lilly Research Laboratories introduces a new oral antibiotic class

THE FIRST CARBASEPHEM

A STEP BEYOND...
NEW CLASS
LORABID™
A STEP BEYOND...
FIRST IN A POTENT
NEW CLASS

A new carbacephem. Combination of benefits.
- Efficacy
- Excellent pharmacokinetic profile
- Safety/tolerance
- B.I.D. DOSING CONVENIENCE

Available in 200-mg Pulvules®
A broad range of clinical indications

Consistent clinical efficacy¹ at the end of treatment in the mild to moderate adult infections you see most often

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
<th>Cured (%)</th>
<th>Improved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary bacterial infection of acute bronchitis</td>
<td>95%</td>
<td>62%</td>
<td>33%</td>
</tr>
<tr>
<td>Acute bacterial exacerbations of chronic bronchitis</td>
<td>93%</td>
<td>54%</td>
<td>39%</td>
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<tr>
<td>Pneumonia</td>
<td>96%</td>
<td>65%</td>
<td>31%</td>
</tr>
<tr>
<td>Acute maxillary sinusitis</td>
<td>97%</td>
<td>65%</td>
<td>32%</td>
</tr>
<tr>
<td>Pharyngitis/tonsillitis</td>
<td>97%</td>
<td>85%</td>
<td>12%</td>
</tr>
<tr>
<td>Uncomplicated pyelonephritis</td>
<td>94%</td>
<td>87%</td>
<td>7%</td>
</tr>
<tr>
<td>Uncomplicated urinary tract infections</td>
<td>90%</td>
<td>84%</td>
<td>6%</td>
</tr>
<tr>
<td>Uncomplicated skin and skin structure infections</td>
<td>93%</td>
<td>67%</td>
<td>26%</td>
</tr>
</tbody>
</table>

¹Clinical efficacy defined as clinical cure or improvement at the end of treatment.

See brief summary of prescribing information on adjacent page.
NEW CLASS
LORACARBEF®
A STEP BEYOND...

Reference

Lorabid® (loracarbef) 200-mg Pulvules®

Brief Summary. Consult the package insert for complete prescribing information.

Indications and Usage: Lorabid is a synthetic β-lactam antibiotic of the cephalosporin class. It is indicated for the treatment of the following mild to moderate infections caused by susceptible strains of designated microorganisms:

Secondary Bacterial Infections of Acute Bronchitis caused by Streptococcus pneumoniae. Non-pneumococcal infections (including β-lactamase-producing strains), or Moraxella (Branhamella) catarrhalis (including β-lactamase-producing strains).

Acute Bacterial Sinusitis caused by S. pneumoniae, H. influenzae (including β-lactamase-producing strains), or S. pyogenes.

Acute Maxillary Sinusitis caused by S. pneumoniae, H. influenzae (including β-lactamase-producing strains only), or M. catarrhalis (including β-lactamase-producing strains).

Pneumonia caused by S. pneumoniae or H. influenzae (non-β-lactamase-producing strains only).

Otitis Media* caused by S. pneumoniae, H. influenzae (including β-lactamase-producing strains), or S. pyogenes (including β-lactamase-producing strains).

Streptococcal pharyngitis.

Adverse Reactions: Most adverse reactions in clinical trials were mild and transient. Only 1.5% of patients discontinued because of drug-related reactions, the most common of which were diarrhea, abdominal pain, and skin rash.

Clinical Studies:

Loracarbef (L) vs β-Lactamase Inhibitor (C) in Acute Otitis Media (US) Efficacy: A study of acute otitis media performed in a population with a higher incidence of β-lactamase-producing organisms than that usually seen in US trials compared loracarbef to amoxicillin. Using very strict evaluative and microbiological clinical response criteria at the 10- to 16-day posttherapy follow-up, the following prescriptive bacterial eradication clinical outcomes (success rates) were obtained:

Pathogen % Due to Pathogen (N = 204) Success Rate
S. pneumoniae 42.6% Equivalent to C
H. influenzae 39.4% 1% less than C
M. catarrhalis 22.9% 1% less than C
S. pyogenes 8.4% Equivalent to C

Safety: The incidences of the most common adverse events were clinically and statistically significantly different in the control group versus the loracarbef group.

Event Loracarbef Control
Diarrhea 1% 13%
Rash* 8% 15%

*Primarily in the diaper area in young children.

Loracarbef (L) vs Amoxicillin (A) in Acute Otitis Media (Europe) Efficacy: A study of acute otitis media performed in a population with a lower incidence of β-lactamase-producing organisms than that usually seen in US trials compared loracarbef to amoxicillin. Using very strict evaluative and microbiological clinical response criteria at the 10- to 16-day posttherapy follow-up, the following prescriptive bacterial eradication clinical outcomes (success rates) were obtained:

Pathogen % Due to Pathogen (N = 291) Success Rate
S. pneumoniae 51.5% Equivalent to A
H. influenzae 71.6% 1% greater than A
M. catarrhalis 15.8% 1% greater than A
S. pyogenes 11.4% Equivalent to A
Overall 100.0% Equivalent to A

Loracarbef (L) vs Doxycycline (D) in Acute Maxillary Sinusitis (Europe) Efficacy: A study of acute maxillary sinusitis performed in a population with a lower incidence of β-lactamase-producing organisms than that usually seen in US trials compared loracarbef with doxycycline. Using very strict evaluative and microbiological clinical response criteria at the 1- to 2-week posttherapy follow-up, the following prescriptive bacterial eradication clinical outcomes (success rates) were obtained:

Pathogen % Due to Pathogen (N = 210) Success Rate
S. pneumoniae 42.7% Equivalent to D
H. influenzae 41.4% 1% greater than D
M. catarrhalis 11.9% Equivalent to D
Overall 98.1% Equivalent to D

Loracarbef (L) vs Cefuroxime (C) in Uncomplicated Cystitis Study (US) Efficacy: A study of cystitis compared loracarbef with cefuroxime. Using very strict evaluative criteria and microbiological clinical response criteria at the 5- to 9-day posttherapy follow-up, the following bacterial eradication rates were obtained:

Pathogen % Due to Pathogen (N = 186) Eradication Rate
E. coli 77.4% 1.4% greater than C
Other major 12.5% Equivalent to C
Enterobacteriaceae 12.5% Equivalent to C
S. saprophyticus 3.8% Equivalent to C

Loracarbef (L) vs Quinolines (Q) in Uncomplicated Cystitis (Europe) Efficacy: A study of cystitis compared loracarbef with an oral quinolone. Using very strict evaluative criteria and microbiological clinical response criteria at the 5- to 9-day posttherapy follow-up, the following bacterial eradication rates were obtained:

Pathogen % Due to Pathogen (N = 188) Eradication Rate
E. coli 82.0% 7% less than Q
Other major 10.1% 3.2% less than Q
Enterobacteriaceae 10.1% 3.2% less than Q
S. saprophyticus 3.8% Equivalent to C

PV 2731 AMP

Additional information available to the profession on request to Eli Lilly and Company, Indianapolis, Indiana 46285.

Eli Lilly and Company
Carolina, Puerto Rico 00985
A Subsidiary of Eli Lilly and Company
Indianapolis, Indiana 46285.
The most widely used calcium antagonist as monotherapy for mild hypertension

- Effective 24-hour control
- Single-agent efficacy
- Well tolerated
- No adverse effects on total cholesterol, plasma glucose levels, renal function, or serum electrolytes

The recommended starting dose for Calan SR is 180 mg once daily. Dose titration will be required in some patients to achieve blood pressure control. A lower initial starting dosage of 120 mg/day may be warranted in some patients (e.g., the elderly, patients of small stature). Dosages above 240 mg daily should be administered in divided doses. Calan SR should be administered with food.

Contraindications: Severe LV dysfunction (e.g., myocardial infarction, severe aortic stenosis, renovascular hypertension), severe bradycardia, hypotension, or severe uncontrolled hypertension.

Warnings: Verapamil should be used with caution in patients with severe LV dysfunction, severe aortic stenosis, or severe uncontrolled hypertension. It may cause a decrease in systolic blood pressure and heart rate. It may also cause a decrease in cardiac output, especially in patients with heart failure or in patients who are taking other medications that can cause bradycardia.

Precautions: Verapamil should be used with caution in patients with severe LV dysfunction or severe aortic stenosis, as it may cause a decrease in heart rate or cardiac output. It may also cause a decrease in systolic blood pressure, especially in patients who are taking other medications that can cause bradycardia.

Adverse Reactions: Constipation, dizziness, nausea, headache, edema, flushing, rash, and injection-site reactions. It may also cause a decrease in heart rate, cardiac output, systolic blood pressure, and renal function.


For the many faces of mild hypertension

Disopyramide should not be given within 48 hours before or after verapamil administration. Concomitant use of disopyramide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined use of verapamil and disopyramide may reduce the therapeutic effect of either drug. It may also cause a decrease in heart rate, cardiac output, systolic blood pressure, and renal function.

Adverse Reactions: Constipation, dizziness, nausea, headache, edema, flushing, rash, and injection-site reactions. It may also cause a decrease in heart rate, cardiac output, systolic blood pressure, and renal function.


For the many faces of mild hypertension


For the many faces of mild hypertension

Triphasil
Levonorgestrel and ethinyl estradiol tablets—Triphasic regimen 21- and 28-day regimens

The OC to start with because she’ll stay with it

- Simple, easy-to-use
- Day 1 Start
- Patient acceptance proven over time*

* Serious as well as minor adverse reactions have been reported following the use of all oral contraceptives. See prescribing information. See brief summary on adjacent page.

FREEDOM FROM PAIN!

Extra strength pain relief free of extra prescribing restrictions.

- Telephone prescribing in most states
- Up to five refills in 6 months
- No triplicate Rx required

Excellent patient acceptance.
In 12 years of clinical experience, nausea, sedation and constipation have rarely been reported.¹

<table>
<thead>
<tr>
<th>COMPARATIVE PHARMACOLOGY OF TWO ANALGESICS</th>
<th>Constipation</th>
<th>Respiratory Depression</th>
<th>Sedation</th>
<th>Vomitus</th>
<th>Physical Dependence</th>
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<tbody>
<tr>
<td>HYDROCODONE</td>
<td>X</td>
<td></td>
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<tr>
<td>OXYCODONE</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
</tbody>
</table>


The heritage of VICODIN,² over a billion doses prescribed.

- VICODIN ES provides greater central and peripheral action than other hydrocodeine/acetaminophen combinations.
- Four to six hours of extra strength pain relief from a single dose
- The 14th most frequently prescribed medication in America²

vicodin ES
(hydrocodone bitartrate 7.5mg [Warning: May be habit forming] and acetaminophen 500mg)

Tablet for tablet, the most potent analgesic you can phone in.

¹ Data on file. Knoll Pharmaceuticals
² Standard industry new-prescription audit

Please see brief summary of prescribing information on adjacent page.
Maintain control of your patient’s therapy.

Rx Specify Do not substitute

Vicodin ES
(hydrocodone bitartrate 7.5mg (Warning: May be habit forming) and acetaminophen 750mg)

It's your prescription – not a suggestion.

INDICATIONS AND USAGE: For the relief of moderate to moderately severe pain. CONTRAINDICATIONS: Hypersensitivity to acetaminophen or hydrocodone. WARNINGS: Respiratory Depression: At high doses or in sensitive patients, hydrocodone may produce dose-related respiratory depression. Head Injury and Increased Intracranial Pressure: The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury or intracranial lesions or in presence of intracranial hypertension. Therefore, narcotics should be prescribed with caution for patients with head injuries or with known or suspected increased intracranial pressure. Apnea: Narcotics produce respiratory depression, which may be more pronounced in the presence of head injury, intracranial lesions or increased intracranial pressure. This respiratory depression is probably caused by a direct depression of the respiration control center in the brainstem. Central Nervous System: In patients treated with narcotics long-term, there is a risk of the development of physical and psychological dependence

9590

Knoll Pharmaceuticals
A Unit of BASF K&F Corporation
Whippany, New Jersey 07981

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V30574-92
Printed in USA
BASF Group
“Today of all days—
I can’t believe
Mom had to get
one of her migraines.”
"I'd give anything
to be with Scott today,
but what could I do?
Between the pain
and the nausea,
I can barely move."

Migraine is more than a headache.
Recent research has revealed that migraine
is a complex, multisymptom disorder of
neurobiological origin. Although various
theories have been proposed regarding the
exact physiological mechanism of migraine,
the practical patient presentation has become
increasingly clear: headache is only one aspect
of the total migraine symptom complex. Nausea,
vomiting, and light and sound sensitivity also
contribute to the disabling nature of migraine.
And that disability means people in the
migraine patient's world suffer too—family,
friends, coworkers.

Current estimates indicate that over 11 million
Americans suffer from migraine with moderate
to severe disability... and the prevalence of
migraine is on the rise. Yet, the sad fact is only
one out of three migraine sufferers is actually
under a physician's care. Many have resigned
themselves to coping on their own.

Fortunately, research may offer
new hope to migraine sufferers.
Results of this research have
given us new
insights into the
neurobiological
basis of migraine... and new hope for
migraine patients.
Unique dual mechanism of action

Controls hypertension through a combination of mild diuresis and vasodilatation.1,2

Gradually reduces both systolic and diastolic blood pressures.3,4

Well-tolerated hypertension control

Low patient dropout rate due to favorable side-effect profile and convenient once-daily dosing.5

Does not adversely affect lipids.6-9

Please see brief summary of prescribing information below.
We set out to write the world's best current therapy book. We succeeded!

The 5-Minute Clinical Consult 1993
H. Winter Griffith, M.D.
Mark D'Ambro, M.D.
450 contributors
About 1400 pp. (8 1/2 x 11), December 1992, $49.50.
ISBN: 0-8121-1593-7

- Over 1000 medical/surgical problems arranged alphabetically and cross-indexed to synonyms of each
- Unique 2-page format designed for rapid retrieval of essential information
- All medication entries and dosages verified by a Pharm.D.
- Annual revisions
- The most coverage on the market
- References listed for additional information and patient education resources
- Full ICD-9 information included
- 90 day examination period

Angina

Basics
- Diagnosis
- Treatment

Medications

FOLLOWUP
- Patient Monitoring
- Prevention/Avoidance

By ignoring the problem, you could raise not only your blood pressure but your risk of heart attack and stroke as well. And once that happens, your number could be up for good. To learn more, contact the American Heart Association, 7272 Greenville Avenue, Box 45, Dallas, TX 75231-4596.

You can help prevent heart disease and stroke. We can tell you how.

American Heart Association

This space provided as a public service. ©1992, American Heart Association
FOR CHRONIC ARTHRITIS

EXPECT A REDUCTION IN JOINT PAIN AND TENDERNESST

Color-enhanced 3-D CT image of OA hip with joint space narrowing and marginal osteophytes. Supplied by David W. Stoller, MD, of California Advanced Imaging.

As with other NSAIDs, the most frequent complaints are gastrointestinal.

Please see brief summary of prescribing information on adjacent page.

EXPECT SUCCESS FROM NAPROSYN®
(NAPROXEN) 500 mg tablets
Also available in 250 and 250 mg tablets and in suspension 125 mg/5 ml.

© 1992 Syntex Puerto Rico, Inc. NP93017
NAPROSYN® (NAPROXEN) 500 mg tablets

Brief Summary

Contraindications: Patients who have had allergic reactions to NAPROSYN®, ANALOXIN® or ANALOX® or of whom aspirin or other NSAIDs induce the syndrome of asthma, urticaria, and nasal polyps. Because anaphylactic reactions usually occur in patients with a history of such reactions, question patients for asthma, nasal polyps, urticaria, and hypodermic associated with NSAIDs before starting therapy. If such symptoms occur, discontinue the drug.

Warnings: Serious GI toxicity such as bleeding, ulceration, and perforation can occur at any time, with or without warning symptoms, in patients treated chronically with NSAIDs. Remain alert for ulceration and bleeding in such patients even in the absence of previous GI tract symptoms. In clinical trials, symptomatic upper GI ulcer, gross bleeding or perforation appeared to occur in approximately 1% of patients treated for 3-4 months, and in about 5.4% of patients treated for 1 year. Inform patients about the signs and symptoms of serious GI toxicity and what steps to take if they occur. Studies have not identified any subset of patients at risk of developing peptic ulceration and bleeding. Except for a prior history of serious GI events and other risk factors known to be associated with peptic ulcer disease, such as alcoholism, smoking, etc., no risk factors (e.g., age, sex) have been associated with increased risk. Elderly or debilitated patients seem to bear ulceration and bleeding less well than others and most spontaneous reports of fatal GI events are in this population. In considering the use of this drug in such patients, the recommended dosage range, sufficient benefit should be anticipated to offset the potential increased risk of GI toxicity. Precautions: Do NOT USE NAPROSYN® (NAPROXEN) CONCURRENTLY WITH ANALOXIN® (NAPROXEN SODIUM) OR ANALOX® 240 mg (NAPROXEN SODIUM) SINCE BOTH CIRCULATE IN PLASMA AS THE NAPROXEN ANION. Acute interstitial nephritis with hematuria, proteinuria, and nephrotic syndrome has been reported. Patients with impaired renal function, heart failure, liver dysfunction, diabetes mellitus, tinnitus, patients taking diuretics, and the elderly are at greater risk of overt renal decompensation if this occurs. Discontinue the drug. Use with caution and monitor serum creatinine and creatinine clearance in patients with significantly impaired renal function. Use caution in patients with baseline creatinine clearance less than 20 mL/min. Use the lowest effective dose in the elderly or in patients with chronic alcoholics, liver disease or cirrhosis. With NSAIDs, borderline elevations of liver tests may occur in up to 10% of patients. They may remain unchanged, or be transient with continued therapy. Elevations of AST or ALT occurred in controlled clinical trials in less than 5% of patients. Severe hepatic reactions, including jaundice and fatal hepatitis, have been reported rarely. If liver disease develops or if systemic manifestations occur (e.g., eosinophilia or rash), discontinue therapy. If steroid dosage is reduced or discontinued, discontinue therapy so slowly and observe patients closely for adverse effects, including adrenal insufficiency and exacerbation of arthritis symptoms. Determine hemoglobin values periodically for patients with initial values of 10 grams or less who receive long-term therapy. Peripheral edema has been reported. Therefore, use with caution in patients with fluid retention, hypertension or heart failure. The drug’s anticoagulant and anti-inflammatory activities may result in fever and inflammation, diminishing their diagnostic value. Conduct echocardiographic studies in any children or infants in whom fever occurs. For patients with restricted sodium intake, note that the suppression of aldosterone is not affected by sodium intake. Patients: Side effects of NSAIDs can cause discomfort and, rarely, there are more serious side effects, such as GI bleeding, which may result in hospitalization and even fatal outcomes. Physicians may have to discuss with patients the potential risks and benefits of NSAID treatment, particularly when they are used for less serious conditions when treated without NSAIDs may be an acceptable alternative. Patients should use caution for activities requiring alertness if they experience dizziness, drowsiness, vertigo, or depression during treatment. Laboratory Tests: Because serious GI tract ulceration and bleeding can occur without warning symptoms, follow chronically treated patients for signs and symptoms of these and inform them of the importance of this follow-up. Drug Interactions: Use with caution when giving concurrently with coumarin-type anticoagulants; a hydantoin, sulfonamide, or sulfinpyrazone; a barbiturate; lithium; propranolol; or metoclopramide. Drug/Laboratory Test Interactions: The drug may increase plasma potassium and increase blood pressure or increase urinary values for 17-ketosteroids. Temporarily stop therapy for 24 hours before doing abnormal function tests. The drug may interfere with urinary assays of SHAM. Carcinogenicity: A 2-year rat study showed no evidence of carcinogenicity. Pregnancy: Category B. Do not use during pregnancy unless clearly indicated. Use with caution in late pregnancy. Nursing Mothers: Avoid use in nursing mothers. Pediatric Use: Single doses of 25-50 mg/kg, with total daily dose not exceeding 10 mg/kg/day, for 3 days in patients weighing 40 kg or less. Adverse Reactions: In a study, GI reactions were more frequent and severe in rheumatoid arthritis patients on 500 mg/day than in those on 750 mg/day. In studies in children with juvenile arthritis, rash and pruritus developing during 3 months were more frequent. GI and CNS reactions about the same, and other reactions less frequent than in adults. Incidence Greater Than 1%. Possible Causal Relationship: GL: The most frequent complaint related to the GI tract: constipation, heartburn, abdominal pain, anorexia, dyspepsia, diarrhea, stomatitis. CNS: headaches, drowsiness, nervousness, light-headedness, vertigo. Dermatologic: rash, pruritus, urticaria, hyperesthesia, urticaria pigmentosa, urticaria, miliaria, pruritus, pruritus ani, pruritus vulvae. Gastrointestinal: anorexia, nausea, vomiting, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anorexia, anor...
In mild to moderate bacterial infections*

**PINPOINTS.**

**PENETRATES.**

**PREVAILS.**

Full-course antibiotic therapy with just 5 once-daily doses

**NEW** Zithromax™

**ONCE DAILY FOR 5 DAYS**

(ZITHROMYCIN) 250-mg capsules

* Due to susceptible strains of indicated organisms.
©1992, Pfizer Inc

Please see adjacent page for brief summary of prescribing information.
For respiratory infections such as acute bacterial exacerbations of COPD (chronic bronchitis) and uncomplicated skin infections: 500 mg single dose on day 1; 250 mg once daily on days 2 through 5. Total dose is 1.5 g.

Zithromax should be given either 1 hour before or 2 hours after a meal.

A favorable safety profile with a low (0.7%; n=4949) discontinuation rate due to side effects. In multidose trials, the most common side effects were diarrhea/loose stools (5%), nausea (3%), and abdominal pain (3%).

References:
"THE GOAL of treating patients with hypertension is to prevent morbidity and mortality associated with high blood pressure."

1988 Joint National Committee
WARNINGS AND PRECAUTIONS. Lopressor
American Medical Television Has Moved to CNBC

Now you can watch American Medical Television Saturday and Sunday on CNBC, the cable arm of the NBC network. The new AMT offers the physician CME programs Saturday and Sunday from 10:00 am-1:00 pm (ET). AMT also offers entertaining health and lifestyle segments for your patients from 1:00 pm-3:00 pm (ET) Saturday and Sunday. That's ten full hours of medical information every weekend! Watching AMT is an enjoyable and convenient way to earn Category I and II CME credits.

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American Medical Television is produced in conjunction with the American Medical Association.
When your patient says she gets cold feet...
When your patient says she gets cold feet...

She may also be saying she has intermittent claudication


Trental® 400 mg Tablets (pentoxifylline)
A brief summary of the prescribing information follows.

INDICATIONS AND USAGE: Trental® (pentoxifylline) is indicated for the treatment of patients with intermittent claudication on the basis of chronic occlusive arterial disease of the limbs. Trental® (pentoxifylline) can improve function and symptoms but is not intended to replace more definitive therapy, such as surgical bypass, or removal of arterial obstructions when treating peripheral vascular disease.

CONTRAINDICATIONS: Trental® (pentoxifylline) should not be used in patients with recent cerebrovascular or retinal hemorrhage, or in patients who have previously exhibited intolerance to this product or methylxanthines such as caffeine, theophylline, and theobromine.

PRECAUTIONS: General: Patients with chronic occlusive arterial disease of the limbs frequently show other manifestations of arteriosclerotic disease. Trental® (pentoxifylline) has been used safely for treatment of patients with occlusive arterial disease of the limbs with concurrent coronary artery and cerebrovascular diseases, but there have been occasional reports of angina, hypotension, and arrhythmia. Controlled trials do not show that Trental® (pentoxifylline) causes such adverse effects more often than placebo, but, as it is a methylxanthine derivative, it is possible that some new adverse effects may occur. Patients should be monitored for adverse hemorrhagic phenomena, which may occur, and the dose reduced if large bleeding occurs. Prolonged use of the drug, in any therapeutic category, should be discontinued in patients with abnormalities of the bleeding time.

Drug Interactions: Although a causal relationship has not been established, there have been reports of bleeding and/or prolongation of prothrombin time in patients treated with pentoxifylline (Trental®) and without anticoagulants or platelet aggregation inhibitors. Patients on warfarin should have more frequent monitoring of prothrombin times while patients with other risk factors complicated by hemorrhage (e.g., recent surgery, peptic ulceration, cerebral and/or retinal bleeding) should have periodic examinations for bleeding including hematocrit and/or hemoglobin.

Nursing Mothers: Pentoxifylline and its metabolites are excreted in human milk. Because of the potential for tumorigenicity shown for pentoxifylline in rats, a decision should be made whether to discontinue nursing or 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 18 years have not been established.

ADVERSE REACTIONS: Clinical trials were conducted using either controlled-release Trental® (pentoxifylline) tablets for up to 60 weeks or immediate-release Trental® (pentoxifylline) capsules for up to 24 weeks. Dosage ranges in the tablet studies were 400 mg bid to tid and in the capsule studies, 200-400 mg tid. The table summarizes the incidence (in percent) of adverse reactions considered drug-related, as well as the number of patients who received controlled-release Trental® (pentoxifylline) and immediate-release Trental® (pentoxifylline) capsules, or the corresponding placebo. The incidence of adverse reactions was higher in the capsule studies (where dose-related increases were seen in digestive and nervous system side effects) than in the tablet studies. Studies with the capsule include domiciliary experience, whereas studies with the controlled-release tablets were conducted outside the U.S. The table indicates that in the tablet studies few patients discontinued because of adverse effects.

INCIDENCE (%) OF SIDE EFFECTS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Controlled-Release Tablets</th>
<th>Immediate-Release Capsules</th>
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<tbody>
<tr>
<td></td>
<td>Commercially Available</td>
<td>Used Only for Controlled Clinical Trials</td>
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<table>
<thead>
<tr>
<th></th>
<th>Trental®</th>
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<tr>
<td>(Number of Patients at Risk)</td>
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<td></td>
</tr>
<tr>
<td>Discontinued for Side Effect</td>
<td>(321)</td>
<td>(128)</td>
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<tr>
<td>Cardiovascular SYSTEM</td>
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</tr>
<tr>
<td>Angina/Chest Pain</td>
<td>0.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Arrhythmia/Palpitation</td>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.6</td>
<td>9.0</td>
</tr>
<tr>
<td>Headache</td>
<td>2.8</td>
<td>4.7</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.2</td>
<td>4.5</td>
</tr>
</tbody>
</table>

| Nervous SYSTEM              |          |         |
| Agitation/Nervousness       | 0.3      | 0.8     |
| Dizziness                   | 1.9      | 3.1     |
| Drowsiness                  | 1.0      | 1.6     |
| Headache                    | 1.2      | 6.2     |
| Insomnia                    | 0.8      | 2.3     |
| Taste                        |          |         |
| Blurred Vision              | 0.3      | 0.8     |
| Edema                       | 0.2      | 0.8     |
| Erythema                    | 0.2      | 0.8     |
| Thrombosis                  | 0.2      | 0.8     |
| SWELLING                    | 0.2      | 0.8     |

OVERDOSAGE: Overdose of pentoxifylline (Trental®) has been reported in children and adults. Symptoms appear to be dose-related. A report from a poison control center on 64 patients taking overdoses of enteric-coated pentoxifylline tablets noted that symptoms usually occurred 4-5 hours after ingestion and lasted about 12 hours. The highest amount ingested was 80 mg/kg. Flushing, hypotension, convulsions, somnolence, loss of consciousness, fever, and agitation occurred. All patients recovered.

In addition to symptoms of treatment and gastric lavage, special attention must be given to supporting respiration, maintaining systemic blood pressure, and controlling convulsions. Activated charcoal has been used to adsorb pentoxifylline in patients who have overdosed.

DOSE AND ADMINISTRATION: The usual dosage of Trental® (pentoxifylline) in controlled-release tablet form is one tablet (400 mg) three times a day with meals.

The effect of Trental® (pentoxifylline) may be seen within 2 to 4 weeks, it is recommended that treatment be continued for at least 8 weeks. Efficacy has been demonstrated in double-blind clinical studies of 6 months' duration. Digestive and central nervous system side effects are dose-related. If patients develop these side effects it is recommended that the dosage be lowered to one tablet twice a day (800 mg/day). If side effects persist at this lower dosage, the administration of Trental® (pentoxifylline) should be discontinued.

Trental® REG TM HOECHST AG Edition 7/91

Hoechst-Roussel Pharmaceuticals Inc.
Somerville, New Jersey (800-729-1296)

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Q3273-192
Patients with intermittent claudication may report other symptoms first:

- Cold feet
- Paresthesia and numbness
- Hair loss and trophic skin changes
- Delayed healing of superficial injuries

You’re most likely to hear them from:

- Patients over 50
- Type II diabetics
- Smokers of more than 25 years
- Hypertensives with elevated triglyceride and depressed HDL levels

TRENTAL® increases pain-free walking distance and improves microcirculatory blood flow:

- Lowers whole blood viscosity
- Increases red cell flexibility
- Lowers red cell aggregation
- Lowers platelet aggregation
- Lowers fibrinogen levels
- Increases white cell flexibility and inhibits neutrophil adhesion and activation

† The clinical significance, if any, of these laboratory findings has not been established.

3 x 3 = Success:

- Patients may improve gradually over 3 months
- The usual dosage of TRENTAL® is one 400-mg tablet 3 times a day, with meals
- Therapy must be continued to sustain improvement

Excellent safety profile:

- TRENTAL® has been used concurrently with antihypertensive, beta-blocker, digitalis, diuretic, antidiabetic and antiarrhythmic regimens without observed problems
- Patients on warfarin should have more frequent monitoring of prothrombin time; periodic systemic blood pressure monitoring is recommended for patients receiving concomitant antihypertensive therapy

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Please see references and brief summary of prescribing information on following page.
FOR PEOPLE WITH ARTHRITIS

THE OBSTACLE COURSE...

THE RECOURSE

Helping overcome life's obstacles

Ansaid®

FLURBI PROFEN

100 Tablets mg

*The average prescribed daily dose is 100 mg bid. Data on file with The Upjohn Company.
As with other nonsteroidal agents, the most frequent side effect is mild gastrointestinal disturbances.

© 1992 The Upjohn Company
For a brief summary of prescribing information, please turn the page.
An effective arthritis treatment, helping to overcome life's obstacles

CONTRAINDICATIONS: Hypersensitivity to Ansaaid, or if aspirin or any other nonsteroidal anti-inflammatory agent induces asthma, urticaria, or other allergic-type reactions. Fatal anaphylactic reactions have been reported in such patients.

WARNINGS: Gastrointestinal effects: Risk of GI ulceration, bleeding, and perforation with nonsteroidal anti-inflammatory drugs. Serious GI toxicity can occur at any time, with or without warning symptoms, during chronic treatment. The occurrence is about 1% after 3 to 6 months, 2% to 4% after a year. Patients should be informed of signs and symptoms of serious GI toxicity and what to do if it occurs. No subset of patients not at risk has been identified. Prior history of serious GI events and other risk factors of peptic ulcer disease, eg, alcoholism, smoking, etc., have been associated with increased risk. The elderly and patients with impaired liver function are more susceptible to drug-induced ulcerations and bleeding; the risk is greater. Ulceration and bleeding can occur with both high and low-dose doses, and chronically treated patients should be followed.

PRECAUTIONS: Patients with impaired renal or hepatic function: Use ANSAID and similar agents cautiously. Pharmacokinetics have not been studied in patients with decreased liver function. Renal function: Rats develop renal papillary necrosis at dosages equivalent to human therapeutic levels, as do monkeys. Changes of up to 10% per hour occur in the same dose. In clinical studies of ANSAID, kidney function tests were done monthly, and renal effects were similar to those seen with other nonsteroidal anti-inflammatory drugs. A second form of renal toxicity has been seen in patients with pre-existing conditions that reduce renal blood flow or volume. A non-steroidal anti-inflammatory drug may cause dose-dependent reduction in prealbumin formation and premature renal decompression. Patients of greatest risk are those with impaired renal or hepatic function, heart failure, those taking diuretics, or the elderly. Drug discontinuation usually leads to recovery. Patients at high risk on chronic treatment should have renal function monitored if they have signs or symptoms that may be consistent with acute tubular necrosis, eg, malaise, fatigue, loss of appetite. Occasionally, BUN and serum creatinine may be elevated without signs or symptoms. Furosemide is excreted by the kidneys, and pharmacokinetics are changed by renal failure; so patients with renal failure should be monitored and may require a reduction of dosage to avoid accumulation of furosemide metabolites. Lives are saved by patients with renal failure, but the dose should be reduced.

Vascular changes: Blurred and/or diminished vision has been reported. With high cortisol levels, patients with complaints should be advised to have periodic ophthalmologic exams. Effects on platelets and hemorrhagic diathesis are rare. Patients should be advised not to take aspirin or other nonsteroidal anti-inflammatory drugs while taking ANSAID, as they may impair platelet aggregation and bleeding time prolonged, patients may be adversely affected should be carefully observed. Information for Physicians: Patients and patients who may wish to discuss potential risks and benefits. Drug interactions: Anticoagulants. Bleeding parameters are affected clinically bleeding is reported. Aspirin plus furosemide levels were 50% lower on concurrent use. Other drugs that may affect bleeding times include: warfarin sodium, heparin, and sulfanilamide. Signs and symptoms suggesting a urinary tract infection: body as a whole: Metabolic:Nonsteroidal Body weight reduction: "Reaction in 3% to 5% of patients. Incidence <1% (Causing relationship probable): Gastrointestinal: Diarrhea, abdominal pain, nausea, vomiting. Central nervous system: Headache, insomnia, irritability, depression, hallucinations, delirium, disorientation, dizziness, weakness, tingling, numbness, tremors, nausea, vomiting. Myocardial infarction, cardiac arrest, arrhythmias, congestive heart failure, angina pectoris. Gastrointestinal: Diarrhea, abdominal pain, nausea, vomiting. Central nervous system: Headache, insomnia, irritability, depression, hallucinations, delirium, disorientation, dizziness, weakness, tingling, numbness, tremors, nausea, vomiting. Myocardial infarction, cardiac arrest, arrhythmias, congestive heart failure, angina pectoris. Gastrointestinal: Diarrhea, abdominal pain, nausea, vomiting. Central nervous system: Headache, insomnia, irritability, depression, hallucinations, delirium, disorientation, dizziness, weakness, tingling, numbness, tremors, nausea, vomiting. Myocardial infarction, cardiac arrest, arrhythmias, congestive heart failure, angina pectoris. Gastrointestinal: Diarrhea, abdominal pain, nausea, vomiting. Central nervous system: Headache, insomnia, irritability, depression, hallucinations, delirium, disorientation, dizziness, weakness, tingling, numbness, tremors, nausea, vomiting. Myocardial infarction, cardiac arrest, arrhythmias, congestive heart failure, angina pectoris.

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The one to consult

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Williams & Wilkins 429 East Preston Street, Baltimore, MD 21202
For the woman at risk...
PREMARIN® 0.625 mg prevents postmenopausal osteoporosis and reduces the risk of hip and wrist fractures by as much as 62%¹

Start early and continue long-term for maximum osteoporosis benefits

Relative risk of hip and wrist fractures in postmenopausal women according to duration of estrogen therapy

62% reduction in risk

Contraindications
Estrogens should not be used in women (or men) with any of the following conditions: known or suspected 1) pregnancy, 2) breast cancer, 3) estrogen-dependent neoplasia, 4) undiagnosed abnormal genital bleeding, 5) active thrombophlebitis or thromboembolic disorders.

Note: Estrogens have been reported to increase the risk of endometrial carcinoma in postmenopausal women.

PREMARIN®
(conjugated estrogens tablets) 0.625 mg

OSTEOPOROSIS
The only cure is prevention

Please see brief summary of prescribing information on next page.
PREMARN® Brand of conjugated estrogens tablets, USP
PREMARN® Brand of conjugated estrogens Vaginal Cream, in a noniiguiting base

1. ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA. Close clinical surveillance of all women taking estrogens is important. Adequate diagnostic measures including endometrial sampling when indicated should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. There is currently no evidence that “natural” estrogens are more or less hazardous than “synthetic” estrogens at equivalent dosages.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY.

Estrogen therapy during pregnancy is associated with an increased risk of congenital defects in the reproductive organs of the male and female fetus, an increased risk of vaginal adenosis, squamous-cell carcinoma of the female cervix, and vaginal cancer in the female fetus in life. The 1965 DES Task Force concluded that women who used DES during their pregnancies may subsequently experience an increased risk of breast cancer. However, a causal relationship is still unproven, and the observed level of risk is similar to that for a number of other breast cancer risk factors.

There is no indication for estrogen therapy during pregnancy. Estrogens are ineffective for the prevention or treatment of threatened or habitual abortion.

DESCRIPTION: PREMARN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from premarin makes urine. It contains estriol, equilen, and 17α-estradiol, together with smaller amounts of 17α-estradiol, equilen, and 17β-estradiol as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available in 6.25 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: Moderate-to-severe perimenopausal symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression which might occur during menopause and they should not be used to treat these conditions.) Prevention and management of osteoporosis (abnormally low bone mass). Al洛tic vaginitis and Atrophic urethritis. Hypoestrogenism due to hypogonadism, castration or primary ovarian failure.

PREMARN (conjugated estrogens) Vaginal Cream is indicated in the management of atrophic vaginitis and pruritic vulv.

PREMARN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

CONTRAINDICATIONS: Estrogens should not be used in women with any of the following conditions: 1. Known or suspected pregnancy (see Boxed Warning). 2. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 3. Known or suspected estrogen-dependent neoplasia. 4. Undiagnosed abnormal vaginal bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. Estrogen replacement therapy has not been reported to increase the risk of thromboembolism and/or thrombocytopenic disease. However, there is insufficient information regarding women who have had previous thromboembolic diseases.

PREMARN Tablets or Vaginal Cream should not be used in patients hypersensitive to their ingredients.

WARNING: These studies suggest a possible increased risk of breast cancer in women taking higher doses of estrogen for prolonged periods. The majority of studies have not shown an association with usual estrogen replacement doses. Endometrial cancer risk among estrogen users is about 4-fold or greater than in non-users, and appears independent of treatment duration and estrogen dose. In patients on combination estrogen-progesterin therapy, this risk appears to be decreased. (See PRECAUTIONS below.)

ESTROGEN THERAPY DURING PREGNANCY is associated with an increased risk of fatal congenital reproductive tract disorders.

A 2.5-fold increase in the risk of surgically confirmed gait bladder disorders in women receiving postmenopausal estrogens has been reported.

Large doses of estrogens such as those used to treat prostates and breast cancer have been shown to increase the risk of non-fatal myocardial infarction, pulmonary embolism, and thromboembolic disease. This cannot necessarily be extrapolated to women. However, to avoid theoretical cardiovascular risk caused by high estrogen doses, the doses for estrogen replacement therapy should not exceed the recommended replacement doses.

Blood pressure should be monitored with estrogen use, especially if high doses are used.

Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: The addition of a progestogen for 7 or more days of a cycle of estrogen administration reportedly lowers the incidence of endometrial hyperplasia. Studies of endometrium suggest that 10 to 13 days of progestin are needed to provide maximal endometrial maturation and elimination of hyperplastic changes. Additional risks: such an adverse effects on carbohydrate and lipid metabolism may be associated with the inclusion of progestin in estrogen replacement regimens. The choice of progestin and dosage may be important in minimizing these adverse effects. Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen and pelvic organs, and should include a Pap smear and mammogram. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention, such as asthma, epispadias, myxedema, and cardiac or renal disease, require careful observation. Certain patients may develop manifestations of excessive estrogen stimulation, such as abnormal or excessive uterine bleeding and mastodynia. Pre-existing uterine leiomyomata may increase in size during estrogen use. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, or metabolic bone diseases associated with hypercalcemia.

The following drug/laboratory test interactions have been reported: some only with estrogen-progesterin combinations (oral contraceptives):

1. Increased methotrexate and factors VIII, VII, IX, and X: decreased antithrombin III; increased nor-epinephrine-induced platelet aggregability.

2. Increased thyroid-binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by Ta3 free levels determined by column or by radioimmunossay. Free Ta3 resin uptake is decreased, reflecting the elevated TBG; free Ta3 concentration is unaltered.

3. Impaired glucose tolerance

4. Reduced response to metyrapone test.

5. Reduced serum folate concentration.

MUTAGENESIS AND CARCINOGENESIS: Long-term, continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver.

PREGNANCY CATEGORY X: Estrogens should not be used during pregnancy. See CONTRAINDICATIONS and BOXED WARNING.

NURSING MOTHERS: As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogen therapy: changes in vaginal bleeding pattern and abnormal withdrawal bleeding or flow through bleeding, spotting, increase in size of uterine fibromyomata, vaginal candidiasis, change in amount of cervical secretion; tenderness or enlargement of breasts; nausea, vomiting, abdominal cramps, bloating, cholestatic jaundice, chills or fever that may persist when drug is discontinued, erythema multiforme, erythema nodosum, hemorraghic eruption, loss of scalp hair, hirsutism; deepening of curvilinear contour, intolerance to contact lenses, headache, migraine, dizziness, mental depression, chorea, increase or decrease in weight; reduced carbohydrate tolerance, aggravation of porphyria; extras changes in libido.

ACUTE OVERDOSE: May cause nausea and vomiting.

DOSAGE AND ADMINISTRATION: PREMARN® Brand of conjugated estrogens tablets, USP.

1. Given cyclically for short-term use only. For treatment of moderate-to-severe vasomotor symptoms, atrophic vaginitis, or atrophic urethritis associated with the menopause (0.3 mg to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off) Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. Given cyclically: Hypoestrogenism. Osteoporosis. Hypoestrogenism due to Female hypogonadism—2.5 mg to 25 mg daily in divided doses for 20 days followed by 10 day rest period. If bleeding does not occur by the end of this period, the same dosage schedule is repeated. Female castration or primary ovarian failure—1.25 mg daily, cyclically Adjust upward or downward according to the response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control. Osteoporosis—0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off).

PREMARN® Brand of conjugated estrogens Vaginal Cream.

2. Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae. The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Attempts to discontinue or taper medication should be made at three- to six-month intervals. (Usual dosage range: 2 g to 4 g daily intravaginally depending on the severity of the condition. Patients with an intact uterus who are treated with either PREMARN Tablets or Vaginal Cream should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

Reference:

Revised August 21, 1989

70662R

Worldwide Leadership in Female Healthcare

Wyeth-Ayerst Laboratories Philadelphia, PA 19101

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It's amazing something this big could fit through a "loophole."

The Americans with Disabilities Act has been law since July 1990. But instead of making their buses accessible, the inter-city bus companies have been making excuses. And somehow they've succeeded in getting themselves a 7-year extension before they even have to begin to comply. When it comes to a little thing like the law, size must make a big difference. Support Easter Seals.
Recent evidence in CHF continues to confirm...

- Improved ejection fraction\textsuperscript{1-3}
- Improved cardiac output\textsuperscript{4,5}
- Improved exercise tolerance\textsuperscript{2,3,6}

...in patients with normal sinus rhythm.

\textbf{IN THE EARLY TREATMENT OF CHF}

\textbf{LANOXIN (digoxin) Tablets}

Unique inotropic support for the failing heart.

Please see brief summary of prescribing information on the following page.
**Improved ejection fraction**

In a large, double-blind, placebo-controlled study of patients in normal sinus rhythm, digoxin produced a significant increase in ejection fraction (P < 0.01) but captropil did not. This improvement results from enhanced myocardial contractile performance and better emptying of the left ventricle.

**Improved cardiac output**

LANOXIN® improves cardiac output at rest as well as during exercise. Maintenance of left ventricular function was clearly demonstrated by a study in which digoxin was withdrawn and then readministered: output deteriorated during withdrawal and was restored during readministration.

**Improved exercise tolerance**

Digoxin improved exercise tolerance by 14% in a double-blind, placebo-controlled study of CHF patients in normal sinus rhythm who underwent treadmill exercise testing (P < 0.03). These gains were achieved in patients receiving baseline diuretics.

Also, in a large study that compared digoxin and captopril, there was no significant statistical difference between the two drugs with regard to their effects on exercise tolerance and functional class.

---

**LANOXIN® (DIGOXIN) TABLETS**

Before prescribing, physicians should be thoroughly familiar with all aspects of this cardiac (or digitalis) glycoside as discussed in the full prescribing information.

**Brief Summary**

**INDICATIONS:**

1. Ventricular fibrillation.
2. An acute, severe and potentially fatal arrhythmia that requires immediate treatment.

**CONTRAINDICATIONS:**

1. Severe pulmonary disease.
2. Severe hepatic disease.
3. Severe renal disease.
4. Severe sepsis.
5. Severe cardiodial failure.

**ADVERSE REACTIONS:**

1. Arrhythmias.
2. Hypo- or hyperglycemia.
3. Hypokalemia.
4. Hyperkalemia.
5. Hypocalcemia.
6. Hypomagnesemia.

**NURSING MATERNITY:**

Studies have shown that the digoxin concentration in the mother's milk is 1% of the plasma concentration.

**DIABETES MELLITUS:**

Studies have shown that the digoxin concentration in the mother's milk is 1% of the plasma concentration.

**PREGNANCY:**

Pregnancy Category C. Animal reproduction studies have not been conducted with digoxin.

**DIURETICS:**

In patients receiving diuretics, digoxin may be initiated at half the usual oral dose.

**CNS:**

Studies have shown that the digoxin concentration in the mother's milk is 1% of the plasma concentration.

**Unique inotropic support for the failing heart.**

---

**Percent Improvement in Exercise Tolerance**

- **Diuretic Baseline:**
  - Digoxin (P < 0.03)
  - Captropil
  - Placebo

- **Adapted from D'Anna et al.**

---

**Percent Improvement in Ejection Fraction**

- **Digoxin (P < 0.05 vs captropil)**
  - NS vs baseline

- **Captopril (P < 0.01 vs placebo)**
  - NS vs baseline

---

**Please see brief summary of prescribing information below.**

---

**References:**

FOR CHRONIC ARTHRITIS

EXPECT A FAVORABLE SAFETY PROFILE

Color-enhanced 3-D CT image of normal stomach. Supplied by David W. Stoller, MD, of California Advanced Imaging.

As with other NSAIDs, the most frequent complaints are gastrointestinal, and rare hepatic and renal reactions have been reported.

Please see brief summary of prescribing information on adjacent page.

EXPECT SUCCESS FROM NAPROSYN
(NAPROXEN) 500 mg tablets
Also available in 375 and 250 mg tablets and in suspension 125 mg/5 mL

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Are you ready to learn what they didn’t teach you in med school?

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Department of Practice Management
515 North State, Chicago, IL 60610

* Please indicate desired areas for information.

Revised: September 1990

Incidence of reported reactions 3%-9%

U.S. patent nos. 3,904,682, 3,998,966 and others.

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Because Fungal Infections Appear In So Many Forms...

A Form To Fit The Therapeutic Need

The NIZORAL (ketoconazole) Family of Products

Outstanding Efficacy...In A Form That Fits
**Microbiology:** Ketoconazole is a broad-spectrum synthetic antifungal agent that inhibits the synthesis of ergosterol in the cell membrane of yeasts and certain fungi. It is active against species of the genera Blastomyces, Coccidioides, Cryptococcus, Histoplasma, Microsporum, and Trichophyton. It may also be active against Toxoplasma gondii and Trichomonas vaginalis. Ketoconazole inhibits the cytochrome P450 enzyme, which is important in the metabolism of many other drugs. This can lead to increased levels of certain medications when taken concurrently with ketoconazole. Therefore, it is important for patients to inform their healthcare providers about all medications they are taking.

**Contraindications and Usage:** Ketoconazole is contraindicated in patients who have demonstrated hypersensitivity to ketoconazole or other members of the imidazole class of antifungal agents. It is also contraindicated in patients with a history of hepatic dysfunction, including liver cirrhosis. ketoconazole is not recommended for use in pregnant women. It is a teratogen and has been associated with fetal abnormalities in animals. It is not known whether ketoconazole crosses the placenta, and its use in pregnant women is not recommended. It is also not recommended for use in children under the age of 12 years.

**Adverse Reactions:** The most common adverse reactions associated with ketoconazole are nausea, vomiting, and diarrhea. Less common reactions include headache, dizziness, drowsiness, and rash. Rare but serious reactions include liver damage, jaundice, and hepatitis. Patients should be monitored for these and other possible adverse reactions.

**Dosage and Administration:** Dosage of ketoconazole is based on the specific indication and the patient's weight. The recommended dose for most indications is 200 mg/day, taken as a single dose or in divided doses. The dose may be increased to 400 mg/day if needed. The duration of therapy varies depending on the indication and the patient's response.

**Precautions:** Patients should be advised of the potential for liver damage and should be monitored for signs of liver dysfunction. They should also be advised to report any symptoms of liver damage, such as jaundice, yellowing of the skin or eyes, or dark urine.

**Nizoral (ketoconazole) 2% Cream**

**Microbiology:** Nizoral is a broad-spectrum synthetic antifungal agent that inhibits the synthesis of ergosterol in the cell membrane of yeasts and certain fungi. It is active against species of the genera Blastomyces, Coccidioides, Cryptococcus, Histoplasma, Microsporum, and Trichophyton. It may also be active against Toxoplasma gondii and Trichomonas vaginalis. Nizoral inhibits the cytochrome P450 enzyme, which is important in the metabolism of many other drugs. This can lead to increased levels of certain medications when taken concurrently with Nizoral. Therefore, it is important for patients to inform their healthcare providers about all medications they are taking.

**Contraindications and Usage:** Nizoral is contraindicated in patients who have demonstrated hypersensitivity to Nizoral or other members of the imidazole class of antifungal agents. It is also contraindicated in patients with a history of hepatic dysfunction, including liver cirrhosis. Nizoral is not recommended for use in pregnant women. It is a teratogen and has been associated with fetal abnormalities in animals. It is not known whether Nizoral crosses the placenta, and its use in pregnant women is not recommended. It is also not recommended for use in children under the age of 12 years.

**Adverse Reactions:** The most common adverse reactions associated with Nizoral are nausea, vomiting, and diarrhea. Less common reactions include headache, dizziness, drowsiness, and rash. Rare but serious reactions include liver damage, jaundice, and hepatitis. Patients should be monitored for these and other possible adverse reactions.

**Dosage and Administration:** Dosage of Nizoral is based on the specific indication and the patient's weight. The recommended dose is 200 mg/day, taken as a single dose or in divided doses. The dose may be increased to 400 mg/day if needed. The duration of therapy varies depending on the indication and the patient's response.

**Precautions:** Patients should be advised of the potential for liver damage and should be monitored for signs of liver dysfunction. They should also be advised to report any symptoms of liver damage, such as jaundice, yellowing of the skin or eyes, or dark urine.

**Janssen Pharmaceuticals**

**Nizoral (ketoconazole) 2% Cream**

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**Contraindications and Usage:** Nizoral is contraindicated in patients who have demonstrated hypersensitivity to Nizoral or other members of the imidazole class of antifungal agents. It is also contraindicated in patients with a history of hepatic dysfunction, including liver cirrhosis. Nizoral is not recommended for use in pregnant women. It is a teratogen and has been associated with fetal abnormalities in animals. It is not known whether Nizoral crosses the placenta, and its use in pregnant women is not recommended. It is also not recommended for use in children under the age of 12 years.

**Adverse Reactions:** The most common adverse reactions associated with Nizoral are nausea, vomiting, and diarrhea. Less common reactions include headache, dizziness, drowsiness, and rash. Rare but serious reactions include liver damage, jaundice, and hepatitis. Patients should be monitored for these and other possible adverse reactions.

**Dosage and Administration:** Dosage of Nizoral is based on the specific indication and the patient's weight. The recommended dose is 200 mg/day, taken as a single dose or in divided doses. The dose may be increased to 400 mg/day if needed. The duration of therapy varies depending on the indication and the patient's response.

**Precautions:** Patients should be advised of the potential for liver damage and should be monitored for signs of liver dysfunction. They should also be advised to report any symptoms of liver damage, such as jaundice, yellowing of the skin or eyes, or dark urine.

**Janssen Pharmaceuticals**

**Nizoral (ketoconazole) 2% Cream**

**Microbiology:** Nizoral is a broad-spectrum synthetic antifungal agent that inhibits the synthesis of ergosterol in the cell membrane of yeasts and certain fungi. It is active against species of the genera Blastomyces, Coccidioides, Cryptococcus, Histoplasma, Microsporum, and Trichophyton. It may also be active against Toxoplasma gondii and Trichomonas vaginalis. Nizoral inhibits the cytochrome P450 enzyme, which is important in the metabolism of many other drugs. This can lead to increased levels of certain medications when taken concurrently with Nizoral. Therefore, it is important for patients to inform their healthcare providers about all medications they are taking.

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**Precautions:** Patients should be advised of the potential for liver damage and should be monitored for signs of liver dysfunction. They should also be advised to report any symptoms of liver damage, such as jaundice, yellowing of the skin or eyes, or dark urine.
A Shape Of Quality

MAXZIDE-25 MG

Potassium and magnesium conservation¹,² with the optimal ratio (1.5 to 1) of triamterene to hydrochlorothiazide³

79% of mildly hypertensive patients normalized* within 4 weeks¹⁺

Twice the bioavailability of Dyazide®³⁺

The Shape to Remember

Once-a-day MAXZIDE®-25 MG
Triamterene 37.5 mg/Hydrochlorothiazide 25 mg

* Diastolic BP < 90 mmHg.
† MAXZIDE-25 MG is indicated for the treatment of hypertension or edema in patients who develop hypokalemia on hydrochlorothiazide alone or in whom the development of hypokalemia cannot be ruled.
‡ Dyazide is a registered trademark of SmithKline Beecham Pharmaceuticals.
© Unique tablet shape is a registered trademark of American Cyanamid Company.
Please see adjacent page for brief summary of full Prescribing Information.
Effectively controls mild-to-moderate hypertension and potassium loss

The Shape to Remember

Once-a-day MAXZIDE-25 MG
Triamterene 37.5mg/Hydrochlorothiazide 25mg

Brief Summary
Please see package insert for full prescribing information.

INDICATIONS AND USAGE
This fixed combination drug is not indicated for the initial therapy of edema or hypertension except in individuals in whom the development of hypokalemia cannot be ruled out.

CONTRAINDICATIONS
Elevated serum potassium levels (0.5-5.0 mEq/L). Discontinue if hypokalemia develops. Concurrent use with other potassium-sparing agents. Concurrent potassium supplementation. Anuria, acute and chronic renal insufficiency, significant renal impairment. Hypersensitivity to either component or to other sulfonamide-derived drugs.

WARNINGS
Hypokalemia. Abnormal elevation of serum potassium levels (0.5-5.0 mEq/L) can occur with all potassium-conserving agents including MAXZIDE. Hypokalemia is more likely to occur in patients with renal impairment, diabetes (even without evidence of renal impairment), or elderly or severely ill patients. The widespread use of thiazide diuretics may be a factor. Serum potassium levels must be monitored at frequent intervals, especially in patients receiving MAXZIDE, when doses are changed, or with any illness that may influence renal function.

Obtain ECG if signs and symptoms of hypokalemia occur. Discontinue MAXZIDE immediately if hypokalemia is present. If the serum potassium level exceeds 6.5 mEq/L, more vigorous therapy is required. Avoid MAXZIDE in diabetic patients. If used, monitor serum electrolytes. Avoid in severe dehydration in patients in whom respiratory or metabolic acidosis may occur. If MAXZIDE is used, frequently evaluate acid/base and serum electrolytes.

Use cautiously, if at all, with agents converting enzyme (ACE) inhibitors. (See PRECAUTIONS, Drug Interactions.)

PRECAUTIONS
Monitor for fluid or electrolyte imbalances at appropriate intervals. Do frequent serum and urine electrolyte determinations (especially when the patient is vomiting or receiving parenteral fluids). Diabetic hyperglycemia may occur in euvolemic patients in hot weather; appropriate therapy is usually water restriction. In actual salt depletion, appropriate replacement is the therapy of choice. Hypokalemia may develop with thiazide therapy, especially with high diuretics. When severe cardiac is present, or during concurrent use of corticosteroids, ACTH, amphetamines, or after prolonged thiazide therapy. Intermittent with adequate oral electrolyte intake will also contribute to hypokalemia. Hypokalemia can accentuate or exaggerate the response of the heart to the toxic effects of digitalis (eg, increased ventricular irritability).

MAXZIDE may produce a lowered blood urea nitrogen level (BUN), creatinine level, or both. Elevations in BUN and creatinine levels may be more frequent in patients receiving diuretic therapy. Discontinue if azotemia increases.

Use with caution in patients with impaired hepatic function or progressive liver disease and in patients with histories of renal lithiasis. Thiazides are a weak, non-acid antiseptics. Periodic blood evaluations are recommended. Hypokalemia may occur or acute glute may be precipitated in certain patients receiving thiazide therapy. The thiazides may decrease serum PBI level without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. Pathological changes in the parathyroid gland with hypokalemia and hypophosphatemia have been observed in a few patients on prolonged thiazide therapy. Discontinue thiazides before conducting tests for parathyroid function.

Insulin requirements in diabetic patients may be changed. Thiazides may cause manifestations of latent diabetes mellitus. Sensitivity reactions to thiazides may occur in patients with or

MAXZIDE and MAXZIDE-25 MG Tablets
Triamterene and Hydrochlorothiazide

without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus by thiazides is possible. Thiazides may add to or potentiate the action of other antihypertensive drugs. Thiazides may decrease apparent responsiveness to nonsteroidal anti-inflammatory agents with MAXZIDE. Use thiazide-sparing agents very cautiously, if at all, in conjunction with angiotensin-converting enzyme (ACE) inhibitors due to a greatly increased risk of hypokalemia. Monitor serum potassium frequently.

MAXZIDE may interfere with glucose measurement. Pregnancy Category C: Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, menstrual irregularities, pancreatitis, and possibly other adverse reactions which have occurred in adults.

Thiazides appear in breast milk. If use is essential, the patient should stop nursing. Adverse reactions are not present in children, nor available.

ADVERSE REACTIONS
Side effects observed in association with the use of MAXZIDE, other combination products containing triamterene/hydrochlorothiazide, and products containing triamterene or hydrochlorothiazide include the following:

Gastrointestinal: nausea, vomiting, cramps, anorexia, diarrhea, constipation, bloating, cramping. Central Nervous System: dizziness, fatigue, insomnia, headache, dizziness, dry mouth, depression, anxiety, vertigo, dizziness, restlessness, delirium. Cardiovascular: tachycardia, flushing, chest pain. Ophthalmic: reduced vision, cataracts, optical changes. Skin: pruritus, rash, urticaria, photosensitivity, dry skin, rash, urticaria, photosensitivity. Other: muscle cramps and weakness, decreased sexual performance and libido. Adverse reactions are not of special significance; therapy should be reduced or withdrawn. Altered Laboratory Findings: Serum Electrolytes: hypokalemia, alkalosis, hypernatremia (see WARNINGS, PRECAUTIONS). Creatinine. Blood Urea Nitrogen: reversible elevations in BUN and serum creatinine have been observed in hypertensive patients treated with MAXZIDE. Glucose: hyperglycemia, hyperuricemia, diabetes mellitus (see PRECAUTIONS). Serum Uric Acid, PBI, and Calcium (see PRECAUTIONS). Other: Elevated liver enzymes have been reported in patients receiving MAXZIDE.

References

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Wayne, New Jersey 07470

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June 1992

8504-21
Drug Evaluations

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THEY WERE CAREFREE...

They were raised in a simpler time, before sugar-free and fat-free. Now hypertension, often with elevated cholesterol and blood sugar, enters the picture...

NOW THEY’RE CONCERNED...
Today's hypertensives with new concerns...

THE CARDURA

*Adapted from the interim (12 months) results of the Treatment of Mild Hypertension Study, a randomized, double-blind, placebo-controlled trial of a nutritional-hygienic regimen along with various drug therapies. All drugs (except acetazolamide) were given initially in low doses. If the patient showed a diastolic blood pressure more than 95 mm Hg on three successive follow-up visits, the dosage was doubled. If blood pressure remained elevated, a second drug (chlordialdione, except for chlordialdione group, which was given eprosartan) was added. Mean diastolic blood pressure was lowered in the various drug groups with median dosages, as follows: doxazosin (2 mg/day), 12.0 mm Hg; enalapril (5 mg/day), 12.2 mm Hg; chlordialdione (15 mg/day), 13.1 mm Hg; and acetazolamide (400 mg/day), 13.7 mm Hg (n=847; P<0.01 vs placebo).

n=128; P<0.01 vs placebo. In a pooled analysis of placebo-controlled studies with about 300 predominantly normocholesterolemic patients per treatment group, CARTRIGHT produced a small decrease in total cholesterol (-2.7%) and LDL cholesterol (-4.3%) and a small increase in the HDL/total cholesterol ratio (+4.3%).

*Adapted from Lehtonen et al* (n=77; after 26 weeks. P<0.01 compared with week 0 for blood pressure and insulin, P<0.05 compared with week 0 for glucose).
Choose CARDURA: first-line therapy for a new generation of hypertensives.

Choose CARDURA for blood pressure control that doesn’t jeopardize blood lipids.

In the Treatment of Mild Hypertension Study, CARDURA lowered diastolic blood pressure (mean 12.0 mm Hg) as effectively as enalapril, chlorthalidone, and acebutolol.¹

CARDURA lowered blood pressure with a small increase in the HDL/total cholesterol ratio (+2.4%)² in the same study.³ The clinical significance of these changes is uncertain. Cholesterol is just one parameter to consider when selecting the best individualized therapy for a given patient.

Choose CARDURA for blood pressure control that doesn’t compromise blood sugar.

CARDURA controlled diastolic blood pressure without an adverse effect on glucose tolerance or insulin control.⁺

CARDURA is well tolerated. In placebo-controlled studies, only three common side effects were reported significantly more often than placebo: dizziness, somnolence, and fatigue.⁵

Only 2% of patients discontinued therapy due to adverse effects—the same as with placebo.

¹ These were generally mild and transient. Syncope has been reported, but rarely (<1%).

---

ONCE-A-DAY CARDURA

(doxazosin mesylate) Scored Tablets 1 mg, 2 mg, 4 mg, 8 mg

HYPERTENSION CONTROL FOR A NEW GENERATION.
CARIDRUM® (doxazosin mesylate) Tablets
Brief Summary of Prescribing Information

INDICATIONS AND USAGE
CARIDRUM may be used alone or in combination with diuretics (often thiazide diuretics) for the treatment of hypertension. In patients without impaired renal function, there is limited experience with CARIDRUM in combination with angiotensin converting enzyme (ACE) inhibitors or calcium channel blockers.

CONTRAINDICATIONS
CARIDRUM is contraindicated in patients with a known sensivity to doxazosin mesylate or to any of its components. Patients with a known history of angioedema, vasculitis, or other similar conditions may not be able to tolerate this medication. CARIDRUM should not be used in patients with impaired renal function (creatinine clearance <30 mL/min), severe congestive heart failure, or severe liver disease. CARIDRUM is also contraindicated in patients with acute coronary syndromes, unstable angina, or severe hypertension.

WARNINGS
Syrup: "First-dose" Effect: Doxazosin, like other alpha-adrenergic blocking agents, can cause marked hypotension, syncope, or other symptoms (including syncope, palpitations, flushing, dizziness, headache, and fainting) in patients with cardiovascular disease, particularly those with severe heart failure, or patients with severe aortic valve disease. When doxazosin is administered, the patient should be warned to avoid activities that require mental alertness and physical coordination, such as driving or operating heavy machinery. Doxazosin should be taken in the morning or evening, with or without food. If the patient experiences dizziness, they should stop activity and remain seated or supine until the dizziness subsides.

PRECAUTIONS
General: Doxazosin is not associated with an increased risk of angina or myocardial infarction. In patients with a history of angina or myocardial infarction, doxazosin should be used with caution and the patient should be observed closely for any signs of deterioration.

Geriatric use: In elderly patients, doxazosin should be used with caution and the dose should be reduced to the lowest effective level. Elderly patients may be more susceptible to hypotension and orthostatic hypotension.

Pregnancy: Doxazosin is contraindicated in pregnant women. However, doxazosin is excreted in human milk. If doxazosin is inadvertently administered to a nursing mother, the patient should be advised to discontinue breastfeeding.

Nursing Mothers: Studies in lactating rats given a single oral dose of 1 mg/kg (2.8 mg/kg) of doxazosin mesylate at weaning (100 mg/kg) to their nursing dams resulted in a decrease in milk production. There is no information on the transfer of doxazosin to human milk. Doxazosin is not recommended for use in pregnant women or nursing mothers.

ADVERSE REACTIONS
Doxazosin mesylate may cause headache, dizziness, drowsiness, nausea, vomiting, diarrhea, constipation, and/or dry mouth. These symptoms usually resolve with continued therapy. Cardiac events such as angina and myocardial infarction are rare but possible. Doxazosin may also cause hypotension, which can lead to syncope or syncopal episodes. Doxazosin has caused a decrease in white blood cell counts.

LABORATORY TEST INTERACTIONS: There is no information on the effect of doxazosin on laboratory test results. However, doxazosin may affect the results of some diagnostic tests, such as those that measure blood pressure or heart rate. Patients should be advised to inform their healthcare provider if they are taking doxazosin.

DRUG/LABORATORY TEST INTERACTIONS: There is no information on the effect of doxazosin on laboratory test results. However, doxazosin may affect the results of some diagnostic tests, such as those that measure blood pressure or heart rate. Patients should be advised to inform their healthcare provider if they are taking doxazosin.

ADDITIONAL REACTIONS: Doxazosin mesylate may cause headache, dizziness, drowsiness, nausea, vomiting, diarrhea, constipation, and/or dry mouth. These symptoms usually resolve with continued therapy. Cardiac events such as angina and myocardial infarction are rare but possible. Doxazosin may also cause hypotension, which can lead to syncope or syncopal episodes. Doxazosin has caused a decrease in white blood cell counts.

RESOURCES:
In NIDDM, when diet alone fails, Glucotrol spells...

Glucotrol (glipizide) 5-mg and 10-mg Scored Tablets

When diet alone fails in non-insulin-dependent diabetes mellitus

As with all sulfonylureas, hypoglycemia may occur.
The reasons to prescribe Glucotrol can pile up fast

Brief Summary of Prescribing Information

INDICATIONS AND USAGE: GLUCOTROL is indicated as an adjunct to diet for the control of hyperglycemia in patients with non-insulin-dependent diabetes mellitus (NIDDM, type II), after an adequate trial of dietary therapy has proven unsatisfactory.

CONTRAINDICATIONS: GLUCOTROL is contraindicated in patients with known hypersensitivity to the drug or with diabetic ketoacidosis, with or without coma, which should be treated with insulin.

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY: The administration of oral hypoglycemic agents has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned in one of four treatment groups (Diabetic, III, suppl. 3, 2747-320, 1979). UGDP reported that patients treated for 12 to 5 years with diet plus a fixed dose of tolbutamide (1.5 gms per day) had a rate of cardiovascular mortality approximately 2.5 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the rate of hyperglycemia was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of GLUCOTROL and of alternative modes of therapy. Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it provides a safe and effective standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS: Renal and Hepatic Disease: The metabolites and excipient of GLUCOTROL may be cleared in patients with impaired renal and/or hepatic function. Hypoglycemia may be prolonged in such patients who should be observed closely.

Hypoglycemia: Euthyroid patients on oral hypoglycemic agents are capable of developing hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemia. Renal or hepatic insufficiency may increase the risk of hypoglycemic reactions. Elderly, debilitated, or unrestrained patients and those with chronic or urinary tract infections are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly or people taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Loss of Control of Blood Glucose: A loss of control may occur in diabetic patients exposed to stress such as fever, trauma, infection, or surgery. It may be necessary to discontinue GLUCOTROL, and administer insulin.

Laboratory Tests: Blood and urine glucose should be monitored periodically. Measurement of glycosylated hemoglobin may be useful.

Information for Patients: Patients should be informed of the potential risks and advantages of GLUCOTROL, of alternative modes of therapy, as well as the importance of adhering to dietary instructions, a regular exercise program, and of regular testing of urine and blood glucose. The roles of hypoglycemia, its symptoms, and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including thiazolidinediones, anti-inflammatory agents, and other drugs that are highly protein bound, salicylates, sulfonamides, thiazides, chlorthalidone, propranolol, colchicine, non-steroidal anti-inflammatory drugs, and digitalis. Since GLUCOTROL reduces the rate of renal tubular excretion of tolbutamide and does not interact with sulfonamides or oral contraceptives, caution should be exercised in prescribing GLUCOTROL in combination with other drugs. However, caution must be exercised in extrapolating these findings to the clinical situation. Certain drugs tend to produce hypoglycemia and may lead to loss of control, including the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid preparations, oral contraceptives, phenytoin, niacin, and sympathomimetics, calcium channel blocking drugs, and heroin. A potential interaction between oral contraceptives and oral hypoglycemic agents leading to septic hypoglycemia has been reported. Whether this interaction also occurs with the intrauterine, topical, or vaginal preparations of norethisterone is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 20-month study in rats and an 18-month study in mice at doses up to 75 times the maximum human dose revealed no evidence of drug-related carcinogenicity. Benadine and an immunological test were uniformly negative. Studies in rats of both sexes at doses up to 75 times the human dose showed no effect on fertility.

Revised August 1990

For more detailed professional information, please visit the Roerig website.
True once-daily antihypertensive control*

Proved by countless patients well controlled on one ISOPTIN SR tablet per day—180 mg or 240 mg—
with virtually no change in metabolic parameters or quality of life 
(total daily doses above 240 mg should be administered in divided doses).

As evidenced by well-controlled, long-term studies at more than 40 US centers. With q.d. dosing, blood pressure was controlled 
**at 24 hours** as demonstrated by a drop in diastolic BP to target levels.

Supported by more than 57,000,000 prescriptions written 
for once-daily verapamil SR† over the past 5.5 years.

**ONCE-DAILY ISOPTIN SR**
(VERAPAMIL HCl)
180/240 mg Sustained-Release Tablets

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*Clinical effectiveness is unrelated to drug plasma levels.
† Constipation is the most frequently reported side effect of ISOPTIN* SR and is easily managed in most patients.
‡ ISOPTIN* SR should be administered with food.
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ONCE-DAILY ISOPTIN® SR (verapamil HCl)
Sustained-Release Tablets
Unsurpassed dosage flexibility

180 mg The recommended starting/maintenance dose
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120 mg For elderly or small stature patients who require lower doses

From the original of verapamil

Knoll Pharmaceuticals
A Unit of BASF K&F Corporation
Whippany, New Jersey 07981

Brief Summary of Prescribing Information

CONTRAINDICATIONS: 1) Severe left ventricular dysfunction (see WARNINGS). 2) Hypotension (less than 90 mm Hg systolic pressure) or cardiogenic shock. 3) Sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker). 4) 2nd or 3rd degree AV block (except in patients with a functioning artificial ventricular pacemaker). 5) Patients with atrial flutter or atrial fibrillation and an accessory bypass tract (e.g., Wolff-Parkinson-White, Long-Ganong-Levine syndromes). 6) Patients with known hypersensitivity to verapamil hydrochloride.

WARNINGS: Heart Failure: ISOPTIN should be avoided in patients with severe left ventricular dysfunction. Patients with milder ventricular dysfunction should, if possible, be controlled before verapamil treatment. ISOPTIN should be avoided in patients with any degree of left ventricular dysfunction if they are receiving a beta adrenergic blocker (see DRUG INTERACTIONS). Hypotension: ISOPTIN (verapamil HCl) may produce occasional symptomatic hypotension. Elevated Liver Enzymes: Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Periodic monitoring of liver function is recommended in patients receiving verapamil; therefore prudent. Accessory Bypass Tract (Wolff-Parkinson-White): Patients with pre-excitation and/or chronic atrial flutter or atrial fibrillation and a connecting accessory AV pathway may develop increased antegrade conduction across the accessory pathway producing a rapid ventricular response or ventricular fibrillation after receiving intravenous verapamil. While this has not been reported with oral verapamil, it should be considered a potential risk (see DRUG INTERACTIONS). Treatment is usually D.C. cardioversion. Atrioventricular Block: The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1st degree AV block and transient bradycardia. Higher degrees of AV block, while infrequent (< 0.8%), may require a reduction in dosage or, in rare instances, discontinuation of ISOPTIN HCl. Patients with Hypertrophic Cardiomyopathy (HCM): Although verapamil has been used in the therapy of patients with HCM, severe cardiovascular decompensation and death have been noted in this patient population.

PRECAUTIONS: Impaired Hepatic or Renal Function: Verapamil is highly metabolized by the liver with about 70% of an administered dose excreted as metabolites in the urine. In patients with impaired hepatic function the dose should be cut to 1/3 of the usual dose and the patient closely monitored. In patients with impaired renal function verapamil should be administered cautiously and the patients monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see OVERDOSE). Use in Patients with Attenuated (Decreased) Neuromuscular Transmission: Verapamil decreases neuromuscular transmission and may prolong recovery from neuromuscular blocking agents. In patients with attenuated neuromuscular transmission lower doses of verapamil may be warranted.

Drug Interactions: Beta Blockers: Concomitant use of ISOPTIN and other beta-adrenergic blocking agents may result in additive negative effects on heart rate, atrioventricular conduction, and/or cardiac contractility. Excessive bradycardia and AV block has been reported. The combination should be used only with caution and close monitoring. Digitalis: Clinical use of verapamil in digitized patients has shown the combination to be well tolerated. However, chronic verapamil treatment increases serum digoxin levels by 50% to 75% during the first week of therapy and this can result in digitalis toxicity. Upon discontinuation of ISOPTIN (verapamil HCl), the patient should be reassessed to avoid underdigitalization. Antihypertensive Agents: Verapamil administered concomitantly with oral antihypertensive agents (e.g., vasodilators, angiotensin-converting enzyme inhibitors, diuretics, alpha and beta adrenergic blockers) will usually have an additive effect on lowering blood pressure. Patients receiving these combinations should be appropriately monitored. Antiarrhythmic Agents: Disopyramide: Disopyramide should not be administered within 48 hours before or 24 hours after verapamil administration. Flecainide: Concomitant administration of flecainide and verapamil may result in additive negative inotropic effect and prolongation of atrioventricular conduction. Quinidine: In patients with hypertrophic cardiomyopathy (HCM), concomitant use of verapamil and quinidine may result in significant hypotension. Other: Nitrates: The pharmacologic profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions. Cimetidine: Variable results on clearance have been obtained in acute studies of healthy volunteers; clearance of verapamil was either reduced or unchanged. Lithium: Pharmacokinetic lowering of serum lithium levels and pharmacodynamic (increased sensitivity to the effects of lithium) interactions between oral verapamil and lithium have been reported. Carbamazepine: Verapamil therapy may increase carbamazepine concentrations and produce related side effects during combined therapy. Ritampin may markedly reduce oral verapamil bioavailability. Phenobarbital: Phenobarbital therapy may increase verapamil clearance. Cyclosporin: Verapamil therapy may increase serum levels of cyclosporin. Anesthetic Agents: Verapamil may potentiate the activity of neuromuscular blocking agents and inhalation anesthetics. Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no evidence of a carcinogenic potential of verapamil administered to rats for two years. Verapamil was not mutagenic in the Ames test. Studies in female rats did not show impaired fertility. Effects on male fertility have not been determined. Pregnancy (Category C): There are no adequate and well-controlled studies in pregnant women. ISOPTIN crosses the placental barrier and can be detected in umbilical venous blood at delivery. This drug should be used during pregnancy, labor, and delivery, only if clearly needed. Nursing Mothers: ISOPTIN is excreted in human milk, therefore, nursing should be discontinued while verapamil is administered. Pediatric Use: Safety and efficacy of ISOPTIN in children below the age of 18 years have not been established.

ADVERSE REACTIONS: Constipation 7.3%, dizziness 3.3%, nausea 2.7%, hypotension 2.5%, headache 2.6%, diarrhea 1.6%, chest pain 1.6%, urticaria 1.4%, 2% and 3% AV block 0.3%, rash 1.3%, flushing 0.9% and elevated liver enzymes (see WARNINGS). The following reactions, reported in less than 1% of patients occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain, they are mentioned to the physician to a possible relationship: angina pectoris, arthroventricular dissociation, arthralgia and pain, blurred vision, cerebrovascular accident, chest pain, clausrophobia, confusion, diarrhea, dry mouth, eczema, erythema, fever, flushing, hypokalemia, impotence, increased urination, insomnia, micturition, muscle cramps, myocardial infarction, palpitations, paresthesias, psychic symptoms, purpura (vasculitis), shakiness, somnolence, spotty menstruation, Steven-Johnson syndrome, sweating, syncope, urticaria.

Treatment of Acute Cardiovascular Adverse Reactions: When severe hypotension or complete AV block occur following oral administration of verapamil, the appropriate emergency measures should be applied immediately: e.g., intravenously administered isoproterenol HCl, levaterenol bitartrate, epinephrine (all in the usual doses), or calcium gluconate (10% solution). Additional support is necessary, isotropic agents (doxapram or dobutamine) may be administered. Actual treatment and dosage should depend on the severity and the clinical situation and the judgment and experience of the treating physician.

OVERDOSAGE: Treatment of overdose should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel and have been used effectively in treatment of severe overdosage with verapamil. Clinically significant hypotensive reactions or fixed high degree AV block should be treated with vasopressor agents or cardiac pacing, respectively. Asystole should be handled by the usual measures including cardiopulmonary resuscitation.

DOSE AND ADMINISTRATION

Essential Hypertension: The dose of ISOPTIN SR should be individualized by titration and the drug should be administered with food. Initiate therapy with 180 mg of sustained-release verapamil HCl, ISOPTIN SR, given in the morning. Lower, initial doses of 120 mg a day may be warranted in patients who may have an increased response to verapamil (e.g., the elderly or small people). Upward titration should be based on therapeutic efficacy and safety reviewed weekly and approximately 24 hours after the previous dose. The antihypertensive effects of ISOPTIN SR are evident within the first week of therapy. If adequate response is not obtained with 180 mg of ISOPTIN SR, the dose may be titrated upward in the following manner:

a. 240 mg each morning
b. 180 mg each morning plus 180 mg each evening, or 240 mg each morning plus 120 mg each evening

c. 240 mg every twelve hours

When switching from immediate release ISOPTIN to ISOPTIN SR, the total daily dose in milligrams may remain the same.
Focus the gray areas of ethical medical practice.

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RELAFEN

For the treatment of osteoarthritis
and rheumatoid arthritis

- Efficacy comparable to naproxen or aspirin

A low incidence of peptic ulcers

- Other G.I. symptoms comparable to
other NSAIDs, including diarrhea (14%),
dyspepsia (13%) and abdominal pain (12%)

Convenient once-a-day dosing

- Usual starting dose 1000 mg/day, taken
as two 500 mg tablets
- Dosage can be titrated up to 2000 mg/day

Please see brief summary of prescribing information on adjacent page.

SmithKline Beecham
Pharmaceuticals
Philadelphia, PA 19101
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RELAFEN®
brand of nabumetone
See complete prescribing information in SmithKline Beecham Pharmaceuticals literature or PDR. The following is a brief summary.

CLINICAL PHARMACOLOGY: Relafen is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic and antipyretic properties in pharmacologic studies. As with other nonsteroidal anti-inflammatory agents, its mode of action is not known. However, the ability to inhibit prostaglandin synthesis may be related to its anti-inflammatory effect. The parent compound is a protonated, which undergoes hepatic biotransformation to the active component, 6-methoxy-2-naphthylacetic acid (6MNA), a potent inhibitor of prostaglandin synthesis.

INDICATIONS AND USAGE: Acute and chronic treatment of signs and symptoms of osteoarthritis and rheumatoid arthritis.

CONTRAINDICATIONS: Patients (i) who have previously exhibited hypersensitivity to it; (ii) in whom Relafen, aspirin or other NSAIDs induce asthma, urticaria or other allergic-type reactions.

WARNINGS: Remain alert for ulceration and bleeding in patients treated chronically, even in the absence of previous GI tract symptoms.

In controlled clinical trials involving 1,677 patients treated with Relafen (1.140 followed for one year and 927 for two years), the incidence of ulcerative signs was 0.56% (95% CI: 0.4%, 0.8%) at three to six months, 0.5% (95% CI: 0.4%, 0.8%) at one year and 0.8% (95% CI: 0.3%, 1.3%) at two years. Inform patients of the signs and symptoms of serious GI toxicity and what steps to take if they occur. In patients with active peptic ulcer, weight loss the benefits of Relafen therapy against possible hazards, institute an appropriate ulcer treatment regimen and monitor the patients’ progress carefully.

Evaluate patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, for evidence of the development of a more severe hepatic reaction while on Relafen therapy. If abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue Relafen. Use Relafen cautiously in patients with severe hepatic impairment.

As with other NSAIDs, use Relafen cautiously in patients with a history of congestive heart failure, hypertension or other conditions predisposing to fluid retention.

Based on U. S. light photosensitivity testing, Relafen may be more phototoxic than aspirin or other NSAIDs, with the potential to result in sun exposure, and may be more likely to result in sun exposure.

In exercising caution when administering Relafen with warfarin since interactions have been seen with other NSAIDs, in two controlled, randomized clinical trials in mice and rats, nabumetone had no statistically significant anticoagulant effect. Nabumetone did not show mutagenic potential in the Ames test and mouse micronucleus test in vivo. Nabumetone did not show chromosomal abnormalities in human lymphocytes in vitro with concentrations up to 800ng/ml, and higher concentrations (equal to the average human exposure to Relafen at the maximum recommended dose).

Nabumetone did not depress fertility of males or female rats treated with doses of 300 mg/kg/day or greater. Pregnancy Category C: nabumetone did not cause any teratogenic effect in rats given up to 400 mg/kg and in rabbits up to 300 mg/kg orally. However, increased postimplantation loss was observed in rats at 100 mg/kg orally and at higher doses (equal to the average human exposure to 6MNA at the maximum recommended human dose). There are no adequate, well-controlled studies in pregnant women. Use the drug during pregnancy only if clearly needed. Because of the known effects of prostaglandin-synthesis-inhibiting drugs on the human fetal cardiovascular system (closure of ductus arteriosus), use of Relafen during the third trimester of pregnancy is not recommended. The effects of Relafen on labor and delivery in women are not known. As with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia and delayed parturition occurred in rats treated throughout pregnancy.

It is not known whether nabumetone or its metabolites are excreted in human milk. However, 6MNA is excreted in the milk of lactating rats. Because of the possible adverse effects of prostaglandin-synthesis-inhibiting drugs on neonates, Relafen is not recommended for use in nursing mothers.

Safety and efficacy in children have not been established.

Of the 1,677 patients in U. S. clinical studies who were treated with Relafen, 411 patients (25%) were 65 years of age or older. 22 patients (14%) were 75 years of age or older. No overall differences in efficacy or safety were observed between these older patients and younger ones. Similar results were observed in a one-year, non-U. S. postmarketing surveillance study of 10,600 Relafen patients, of whom 4,577 patients (43%) were 65 years of age or older.

ADVERSE REACTIONS: Incidence ≥1%—Probable Cause Related—Diarrhea (14%), dyspepsia (13%), abdominal pain (12%), constipation (12%), flatulence (11%), nausea (11%), skin rash (11%), vomiting (11%), edema (10%), pruritus* (10%), deterrent*, etc.

Incidence ≤1%—Probable Cause Related—Anorexia (9%), cholecystitis (9%), duodenal ulcer (9%), gastritis, hemorrhage, gastroesophageal bleeding, increased appetite, liver function abnormalities, melena (9%), pancreatitis, depression, ecchymosis, insomnia, increased sweating, rash, urticaria, etc.

*Incidence of reported reaction between 3% and 9%. Reactions occurring in 1% to 3% of the patients are unreported.

Incidence ≤1%—Probable Cause Related—Anemia* (9%), cholestasis (9%), dermatitis (9%), dyspepsia (9%), dysuria, rash, sweating, thirst, taste disturbances, urticaria (9%), vomiting (9%), etc.

Incidence ≤0.1%—Probable Cause Related—Aspiration (9%, 9%), bullous dermatitis (9%), candidiasis, gingivitis, glossitis, herpes simplex, loss of hair, neutropenia, perioral dermatitis, pruritus, rash, Stevens-Johnson Syndrome (9%), urticaria (9%), vascular headache, paresthesia, photosensitivity, arthralgia, pseudoephedrine cutaneous reactions, myalgia, fatigue, loss of hair, lymphadenopathy, anemia, chest pain, nausea, diarrhea, palpitations, cough, dyspnea, urticaria, impotence, renal stones, taste disorder, fever, chills, anemia, leukopenia, granulocytopenia, thrombocytopenia, hypothermia, anaphylaxis, weight loss, dysuria, rash, pruritus, hypokalemia, fever, drug fever, etc.

Adverse reactions reported in preclinical studies or postmarketing experience or in the literature are listed.

OVERDOSAGE: If acute overdose occurs, empty the stomach by vomiting or lavage and institute general supportive measures as necessary. Activated charcoal, up to 60 grams, may effectively reduce nabumetone absorption. Co-administration of ranitidine with charcoal to man has resulted in an 80% decrease in maximum plasma concentrations of the active metabolite.

One overdose occurred in a 27-year-old female patient who had a history of abdominal pain and was hospitalized for increased abdominal pain following ingestion of 30 Relafen tablets (15 grams total). Stools were negative for occult blood and the patient had no lab abnormalities suggestive of abnormalities. The patient did not have any other symptoms. She was given an H2 receptor antagonist and discharged from the hospital without sequelae.

DOSAGE AND ADMINISTRATION: Recommended starting dose: 1000 mg taken as a single dose with or without food. Some patients may obtain more symptomatic relief from 1500 mg to 2000 mg daily. Doses over 2000 mg daily have not been studied. Use the lowest effective dose that controls symptoms. If you’re looking for some good reading, you’ve just found it. The free Consumer Information Catalog.

The Catalog lists about 200 federal publications, many of them free. They can help you eat right, manage your money, stay healthy, plan your child’s education, learn about federal benefits and more.

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  - *H. influenzae*, *S. pneumoniae*,
  - *S. pyogenes*, *M. catarrhalis*
  - and *M. pneumoniae*¹⁻⁴

- Excellent tissue penetration without sacrificing therapeutic serum levels¹⁻⁵

*Due to susceptible strains of indicated organisms.*

Clinical success rate: clinical cure or improvement within 4-6 days post-treatment.

¹Please see following page for brief summary of Prescribing Information.
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- Excellent clinical success rates in community-acquired pneumonia, acute exacerbation of chronic bronchitis, pharyngitis, tonsillitis, and acute maxillary sinusitis

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- Unique once-daily convenience
- Comfortable delivery—very low incidence of nasal irritation
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- Early morning mean serum cortisol levels remained comparable to baseline throughout a 2-year study

Simplifies dosing
Extends relief

*In doses up to 440 mcg/day.
Please see next page for brief summary of prescribing information.
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THE ONCE-DAILY NASAL STEROID
ONCE DAILY Nasacort Nasal Inhaler
(triamcinolone acetonide)

[Image: Nasacort Nasal Inhaler]

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

WARNINGS: The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency and, in addition, some patients may experience symptoms of withdrawal, e.g., joint and/or muscular pain, lactation and depression. Patients previously treated for prolonged periods with systemic corticosteroids may present in adrenal crisis when treatment is interrupted. These patients should be carefully monitored for acute adrenal insufficiency in response to stress. In those patients who have asthma or other clinical conditions requiring long-term systemic corticosteroid treatment, too rapid a decrease in systemic corticosteroids may cause a severe exacerbation of their symptoms.

The use of Nasacort Nasal Inhaler with alternate-day systemic prednisone could increase the likelihood of hypothalamic-pituitary-adrenal (HPA) suppression compared to a therapeutic dose of either one alone. Therefore, Nasacort Nasal Inhaler should be used with caution in patients already receiving alternate-day prednisone treatment for any disease.

PRECAUTIONS

GENERAL: In clinical studies with triamcinolone acetonide administered intranasally, the development of localized infections of the nose and pharynx with Candida albicans has rarely occurred. When such an infection develops it may require treatment with appropriate local therapy and discontinuance of treatment with Nasacort Nasal Inhaler.

Nasacort Nasal Inhaler should be used with caution. If, at all, in patients with active or quiescent tuberculosis infections of the respiratory tract or in patients with untreated fungal, bacterial, or systemic viral infections or ocular herpes simplex. Because of the inhibitory effect of corticosteroids on wound healing in patients who have experienced recent nasal septal ulcers, nasal surgery, or trauma, a corticosteroid should be used with caution until healing has occurred.

When used at excessive doses, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, Nasacort Nasal Inhaler should be discontinued, slowly, consistent with accepted procedures for discontinuing oral steroid therapy. See Information for Patients for further information.

Patients should use Nasacort Nasal Inhaler at regular intervals since its effectiveness depends on its regular use. A decrease in symptoms may occur as soon as 12 hours after starting therapy and generally can be expected to occur within a few days of initiating therapy in allergic rhinitis. The patient should take the medication as directed and should not exceed the prescribed dosage. The patient should contact the physician if symptoms do not improve after three weeks, or if the condition worsens. Nasal irritation and/or burning or stinging after use of the spray occur only rarely with this product. The patient should contact the physician if these symptoms occur.

For the proper use of this unit and to attain maximum improvement, the patient should read and follow the accompanying patient instructions carefully. Because the amount dispensed per puff may not be consistent, it is important to shake the canister well. Also, the canister should be discarded after 100 actuations.

Carcinogenesis, Mutagenesis: Animal studies of triamcinolone acetonide to test its carcinogenic potential are underway.

Impairment of Fertility: Male and female rats which were administered oral triamcinolone acetonide at doses as high as 150 mg/kg/day (110 mcg/m2/day, as calculated on a surface area basis) exhibited no evidence of impaired fertility. The maximum human dose, for comparison, is 6.3 mg/kg/day (340 mcg/m2/day). However, a few female rats which received maternal triamcinolone acetonide doses of 8 or 15 mg/kg/day (50 or 110 mcg/m2/day, respectively, as calculated on a surface area basis) exhibited dystocia and prolonged delivery. Developmental toxicity, which included increases in fetal resorptions and stillbirths and decreases in pup body weight and survival, also occurred at the maternally toxic doses (8 - 15 mcg/m2/day, as calculated on a surface area basis). Reproductive performance of female rats and effects on males and offspring were comparable between groups that received placebo and non-toxic or marginally toxic doses (0.5 and 1.0 mcg/kg/day or 3.8 mcg/m2/day and 7.6 mcg/m2/day).

Pregnancy: Pregnancy Category C. Like other corticoids, triamcinolone acetonide has been shown to be teratogenic in rats and rabbits. Teratogenic effects, which occurred in both species at 0.02, 0.04 and 0.06 mg/kg/day (approximately 12.5, 25 and 50 mcg/m2/day in the rat and 110, 220 and 330 mcg/m2/day in the rabbit, as calculated on a surface area basis), included a low incidence of cleft palate and/or posterior hypoplasia and axial skeletal defects. Teratogenic effects, including CNS and cranial malformations, have also been observed in non-human primates at 0.05 mg/kg/day (approximately 7 mg/m2/day). The doses of 0.04, 0.06, and 0.05 mg/kg/day used in these teratology studies are approximately 12.5, 25 and 50 times (110, 220 and 330 mcg/m2/day in the rat and 3.2, 3.6 and 4 times 110, 220 and 330 mcg/m2/day in the rabbit), the minimum recommended dose of 110 mcg of Nasacort per day and 5.8, 6.4 and 7 times the minimum recommended dose of 110 mcg of Nasacort per day based on a patient body weight of 70 kg. Administration of aerosol by inhalation to pregnant rats and rabbits produced embryotoxic and fetal effects which were comparable to those produced by administration by other routes. There are no adequate and well-controlled studies in pregnant women. Triamcinolone acetonide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Experience with oral corticoids since their introduction in pharmacologic as opposed to physiologic doses suggests that rodents are more prone to teratogenic effects from corticoids than humans. In addition, because there is a natural increase in glucocorticoid production during pregnancy, most women will require a lower exogenous steroid dose and many will not need corticosteroid treatment during pregnancy.

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

Nursing Mothers: It is not known whether triamcinolone acetonide is excreted in human milk. Because other corticosteroids are excreted in human milk, caution should be exercised when Nasacort Nasal Inhaler is administered to nursing women.

Pediatric Use: Safety and effectiveness have not been established in children below the age of 12. Oral corticosteroids have been shown to cause growth suppression in children and teenagers, particularly with higher doses over extended periods. If a child or teenager on any corticosteroid appears to have growth suppression, the possibility that they are particularly sensitive to this effect of steroids should be considered.

ADVERSE REACTIONS: In controlled and uncontrolled studies, 1257 patients received treatment with intranasal triamcinolone acetonide. Adverse reactions are based on the 567 patients who received a product similar to the marketed Nasacort inhaler. These patients were treated for an average of 56 days (range 1 to 117 days). The 145 patients enrolled in uncontrolled studies received treatment from 1 to 820 days (average 355 days). The most prevalent adverse experience was headache, being reported by approximately 11% of the patients who received Nasacort. Nasal irritation was reported by 2.5% of the patients receiving Nasacort. Other nasopharyngeal side effects were reported by fewer than 5% of the patients who received Nasacort and included dry mucous membranes, naso-sinus congestion, throat discomfort, sneezing, and epistaxis. The complaints do not usually interfere with treatment and in the controlled and uncontrolled studies approximately 1% of patients have discontinued because of these nasal adverse effects.

In the event of accidental overdose, an increased potential for these adverse experiences may be expected, but systemic adverse experiences are unlikely (see OVERDOSAGE section).

OVERDOSAGE: Acute overdosage with this dosage form is unlikely. The acute topical application of the entire 15 mg of the canister would most likely cause nasal irritation and headache. It would be unlikely to see acute systemic adverse effects if the nasal application of the 15 mg of triamcinolone acetonide was administered all at once.

Cautions: Federal (U.S.A.) law prohibits dispensing without prescription. Please see product circular for full prescribing information.


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The American Medical Association Proudly Announces...

Healthy Youth 2000

In cooperation with the American Academy of Pediatrics

A campaign to promote better health for the youth of America
American Medical Association

Physicians dedicated to the health of America

Dear Colleague:

Since the American Medical Association was founded in 1847, we have been committed to promoting the health and welfare of all our citizens. **HEALTHY YOUTH 2000** is an educational program that embodies this commitment by focusing on a segment of our population that is at special risk: the youth of America.

**HEALTHY YOUTH 2000** is part of the AMA's effort in support of HEALTHY PEOPLE 2000, a broad-based plan designed by the U.S. Public Health Service to increase the span of healthy life for all Americans. The AMA's involvement in this program is further proof that our concern for our patients' welfare does not end when they leave our offices.

James S. Todd, M.D.
Executive Vice President
Healthy Youth 2000: The Challenge.

Childhood and adolescence are critical times for healthy human development. Not only are children dependent on other individuals for their food, clothing, and protection, but they are influenced by the behavioral patterns that they witness. The vulnerability of children places them at special risk for many preventable problems.

Adolescence is a time of rapid physical and emotional change, a period of learning and experimentation. Attitudes and behaviors that are developed in adolescence, related to diet, exercise, sexual practices, safety habits, tobacco, and alcohol use, may have health consequences that continue through adulthood.

As physicians, our potential opportunities for positive interventions with our patients begin with contacts prior to conception and continue throughout pregnancy, childhood, and adolescence.

Studies have clearly documented the value of the medical care we provide. Prenatal care and immunization programs are proven, cost-effective activities. No less valuable are the advice and encouragement we give to parents and caregivers and, ultimately, to youth themselves. The need for health counseling is especially important for adolescents as they confront rapid physical, emotional, and behavioral changes. These are necessary tools to ensure that the youth of America achieve a maximum level of health and function.

Nutrition
- Reduce the prevalence of overweight among children and adolescents.
- Insure adequate calcium intake among children and adolescents.
- Increase the proportion of young people who use food labels to make nutritious food selections.

Unintentional Injuries
- Reduce deaths among youth aged 15 through 24 caused by motor vehicle crashes.
- Reduce drowning deaths among children and young adults.
- Increase the use of helmets among motorcyclists and bicyclists.
- Increase the use of automobile safety seats and seatbelts for children.
HEALTHY YOUTH 2000 is an educational program designed to promote better health for the youth of America. The program will provide educational materials for health professionals, patients, and the general public.

PHYSICIAN INVOLVEMENT
Active physician involvement is the key to success for HEALTHY YOUTH 2000. Participating physicians will receive educational materials for use by parents, other caregivers, and youth themselves. All physicians will have access to the campaign’s CME programs and to regular updates through AMA publications, mailings, and American Medical Television.

PATIENT EDUCATION IN YOUR OFFICE
The physician's office provides an ideal environment for distributing educational materials to parents, other caregivers, and youth. Participating physicians will receive free educational brochures and posters about immunization, nutrition, physical fitness, safety and other health issues affecting youth. Their patients will enjoy special access to AMA-approved books and videos designed to enhance the health of our youth.

OBJECTIVES

PHYSICAL ACTIVITY AND FITNESS
- Increase the proportion of children and young adults who engage in vigorous physical activity that promotes the development and maintenance of cardiorespiratory fitness 3 or more days per week for 20 or more minutes per occasion.
- Reduce the proportion of people aged 6 and older who engage in no leisure-time physical activity.

ORAL HEALTH
- Reduce dental cavities so that the proportion of children with one or more cavities is no more than 60% among adolescents aged 15.

ENVIRONMENTAL HEALTH
- Reduce asthma morbidity among children aged 14 and younger, as measured by a reduction in asthma hospitalizations.
**ACTION PLAN.**

**PUBLIC EDUCATION**

_Healthy Youth 2000_ will use national and local television to inform the public about youth health subjects. The campaign will provide medical editors and writers with the facts they need to report accurately and responsibly on these subjects.

Your patients will receive useful, health-promoting information from the campaign in their newspapers, national magazines, and the AMA's own publication _Living Well_. These messages will promote healthy lifestyles for our youth, and remind parents of the need for and availability of preventive medical care. The AMA will also work with the publishers of classroom materials to deliver health-promoting information directly to America's youth.

**NATIONAL SPONSORS**

National sponsors will support the educational goals of _Healthy Youth 2000_ through messages on their products, in their advertising, and by the distribution of millions of informational brochures. Sponsor support will also enable consumers to obtain AMA-approved books and videos at substantial discounts. The scientific content of all sponsored messages and materials will be completely controlled by the AMA.

Campaign sponsors include:

- **MERCK**
  - Vaccine Division

- **ROSS PEDIATRICS**

- **Cheerios**
  - Good Housekeeping

- **Parents Magazine**

- **HOME**

**OBJECTIVES**

**TOBACCO**

- Reduce the initiation of cigarette smoking by children and youth.

- Reduce smokeless tobacco use by males.

**ALCOHOL AND OTHER DRUGS**

- Reduce deaths among people aged 15 through 24 caused by alcohol-related motor vehicle crashes.

- Reduce the proportion of young people who use alcohol, marijuana, and cocaine.

- Reduce the proportion of high school seniors and college students engaging in heavy drinking of alcoholic beverages.

**MENTAL HEALTH AND MENTAL DISORDERS**

- Reduce suicides among youth aged 15 through 19.

- Increase access to mental health services for children and adolescents.
The success of the AMA's **HEALTHY YOUTH 2000** program depends on the active involvement of people from many sectors of life, including physicians, nurses, dentists, pharmacists, health educators, hospitals and a wide variety of professional organizations. Opportunities for involvement range from simple distribution of patient education materials to active participation in educational activities at community, regional and national levels.

To enroll, simply complete and return the following enrollment form.

---

**Yes! Enroll me in the AMA's HEALTHY YOUTH 2000.**
**Please send me an official kit for my practice. I understand the kit includes patient education materials.**

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Please send _additional kits (one for each doctor in our practice)._

☐ Check here if you want your kit(s) to be bilingual (Spanish and English).

☐ Check here to receive membership information from the American Medical Association and/or the American Academy of Pediatrics.

**Mail To:**

**HEALTHY YOUTH 2000**
3575 Cahuenga Blvd. West, Suite 400
Los Angeles, CA 90068
HEALTHY YOUTH 2000 is the fourth in a series of national health promotion campaigns conducted by the American Medical Association since 1988. The campaigns are designed to help all Americans live healthier lives.

- 60,000 physicians enlisted in the Campaign.
- Millions of brochures were distributed in physician offices.
- 70,000 physicians participated in CME activities.
- Millions of Americans were screened for high blood cholesterol.
- The AMA's 5-week Cholesterol Reduction course was licensed to more than 190 hospitals.
- Two prime-time specials and 54 short segments were syndicated to 118 TV stations.
- 27 million readers used two special editorial inserts printed in Good Housekeeping.
- National Sponsors delivered over 500 million messages to American households.
- Campaign messages were displayed in supermarkets across the country.

- 25,000 physicians enlisted in the Campaign.
- Millions of brochures were distributed in physician offices.
- 75,000 physicians participated in CME activities.
- Two 5-part reports on national television were tied in with editorial inserts in Good Housekeeping.
- A national Health Reporters Conference produced extensive coverage in the media.
- "Walks for Women's Health" were held in 21 cities.
- National Sponsors delivered some 400 million messages to American households.

- 20,000 physicians enlisted (activity ongoing).
- Millions of brochures are currently being distributed in physician offices.
- Advertorial inserts in six issues of American Medical News and JAMA to more than 350,000 physicians.
- An 8-part report on ABC's HOME Show tied in with 10 million educational inserts in Good Housekeeping and Parade.
- A National Media Seminar resulted in extensive media coverage.
- The AMA's smoking cessation program was released in video format.

To enroll in HEALTHY YOUTH 2000 – Return form at left
Fast, effective relief for pain/inflammation.

- Sprains/Strains
- Acute tendinitis/Bursitis
- Low back pain
- Musculoskeletal pain
- Soft-tissue trauma
**Fast**—pain relief may occur as fast as 20 minutes.

**Effective**—works at the pain site to provide relief for mild to moderate pain/inflammation.

**Anti-inflammatory**—nonsteroidal anti-inflammatory action helps patients return to normal activity.

**Well tolerated**—no narcotic-related side effects; no addiction potential.

As with other NSAIDs, the most frequent complaints are gastrointestinal. See Warnings, Precautions, and Adverse Reactions sections of prescribing information.

**Convenient dosing**—recommended starting dose is 550 mg, followed by 275 mg every 6 to 8 hours, as required. Total daily dose should not exceed 1375 mg.

---

**Fast Relief. Fast Recovery.**

550 MG TABLETS

Anaprox® DS

275 MG TABLETS

Anaprox®

(NAPROXEN SODIUM)

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SYNTEX

© 1992 Synthex Puerto Rico, Inc. 811-J2-505-92

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For brief summary of prescribing information, please see next page.
Facilitates renal function.
- No clinically significant change in serum creatinine or creatinine clearance.
- No clinically significant effect on glomerular filtration rate.
- Maintains or decreases filtration fraction.

Maintains cardiac performance.
- No significant effect on heart rate.
- No adverse effect on cardiac conduction or contractility.
- No alteration of digoxin clearance.

Does not compromise metabolic parameters.
- No clinically significant effect on serum glucose metabolism.
- No effect on glucose tolerance, insulin secretion, or insulin action in NIDDM patients.
- No clinically significant effect on lipid metabolism.
- No known contraindications except for hypersensitivity to DynaCirc
- No significant interactions with the 20 most-commonly prescribed drugs
- Effectively reduces diastolic and systolic blood pressure without orthostatic hypotension
- Side effects are usually minimal and transient
  - Low incidence of edema: 3.5% at 2.5 mg b.i.d. and 8.7% at 5 mg b.i.d.
  - Rare incidence of constipation or cough (<1%)
  - Headache (12.6%) and dizziness (8.0%) are the most frequently reported side effects at 2.5 mg twice a day
- Among the least expensive calcium channel blockers

*D Mild, clinically insignificant increases in heart rate may occur occasionally.
† In limited studies, no adverse effect was seen on cardiac index and other indirect measurements of contractility in patients with normal function or moderate left ventricular dysfunction. However, caution should be exercised when using the drug in patients with CHF, particularly in combination with a beta blocker. Isradipine has a negative inotropic effect at high doses in vitro. In addition, some patients may have increased clinical consequences of these effects that have not been evaluated.
§ Prescribed to patients aged 55 and above. Data from PDDA Top 100 Drugs: Uses for Dec 1990- Nov 1991, excluding calcium channel blockers.
¶ Initial therapy with higher than recommended doses may cause orthostatic hypotension in patients with severe CHF.
¶ At recommended doses of 2.5 to 5 mg b.i.d.

DynaCirc®
(isradipine)
2.5 mg capsules
(5 mg capsules)

For Safety's Sake™

Please see following page for brief summary of full Prescribing Information.
INDICATION
Dynacirc® (isradipine) is indicated in the management of hypertension. It may be used alone or concurrently with thiazide-type diuretics.

CONTRAINDICATIONS
Dynacirc® is contraindicated in individuals who have shown hypersensitivity to any of the ingredients in the formulation.

WARNINGS
None.

PRECAUTIONS
General: Blood Pressure: Because Dynacirc® decreases peripheral resistance, like other calcium blockers Dynacirc® may occasionally produce symptomatic hypotension. However, symptomatic and syncope-like syndrome is extremely rare and experienced in hypotensive patients administered Dynacirc®, particularly at the initial recommended dose. Use in Patients with Congestive Heart Failure: Although acute hemodynamic studies in patients with congestive heart failure have shown that Dynacirc® does not reduce afterload without impairing myocardial contractility, it has a negative isotropic effect at high doses in vitro, and possibly in some patients. Caution should be exercised when using the drug in congestive heart failure patients, particularly in combination with a beta-blocker.

Drug Interactions: Nitroglycerin: Dynacirc® has been safely coadministered with nitroglycerin. Hydrochlorothiazide: A study in normal healthy volunteers has shown that coadministration of Dynacirc® and hydrochlorothiazide does not alter antihypertensive response of either drug. In a study in hypertensive patients, addition of isradipine to existing hydrochlorothiazide therapy did not result in any unexpected adverse effects, and isradipine had an additional antihypertensive effect.

Propanolol: In a single dose study in normal volunteers coadministration of propanolol had a small effect on the rate but no effect on the extent of isradipine bioavailability. Coadministration of Dynacirc® resulted in significant increases in AUC (27%) and Cmax (58%) and decreases in t1/2 (23%) of propranolol. Digoxin: The concomitant administration of Dynacirc® and digoxin in a single-dose pharmacokinetic study did not affect renal, nonrenal and total body clearance of digoxin. Fentanyl/Anesthesia: Severe hypotension has been reported during fentanyl anesthesia with concomitant use of a beta-blocker and a calcium channel blocker. Even though such interactions have not been seen in clinical studies with Dynacirc®, an increased volume of circulating fluids might be required if such an interaction were to occur. Carcinogenesis, Mutagenesis, Impairment of Fertility: Treatment of male rats for 2 years with 2.5, 12.5, or 62.5 mg/kg/day isradipine admixed with the diet resulted in dose dependent increases in the incidence of benign Leydig cell tumors and testicular hyperplasia relative to untreated control animals. A comparable endocrine effect was not evident in male patients receiving therapeutic doses of the drug on a chronic basis.

ADVERSE REACTIONS
The adverse reaction rates given below are principally based on controlled hypertension studies; but rarer serious events are derived from all exposures to Dynacirc® including foreign marketing experience. Most adverse reactions were mild and related to the vasodilatory effects of Dynacirc® (dizziness, edema, palpitations, flushing, tachycardia), and many were transient. About 5% of isradipine patients left studies prematurely because of adverse reactions (vs. 3% of placebo patients and 6% of active control patients), principally due to headache, edema, dizziness, palpitations, and gastrointestinal disturbances. The following adverse reactions have been reported by 1% or greater of patients receiving Dynacirc® at any dose (N=9344): headache (13.7%), dizziness (7.3%), edema (7.2%), palpitations (4.5%), fatigue (3.9%), flushing (2.5%), chest pain (2.4%), nausea (1.8%), dyspepsia (1.8%), abdominal discomfort (1.7%), tachycardia (1.5%), rash (1.5%), polkauria (1.5%), weakness (1.2%), vomiting (1.1%), diarrhea (1.1%). The following adverse events were reported in 0.2-1.2% of the isradipine-treated patients in hypertension studies, or are rare, but more serious events from this and other data sources, including postmarketing exposure, are being closely monitored.


[DECEMBER 31, 1990 DYN-Z2]
We're Expanding Our World So You Can Expand Yours

American Medical Television has joined CNBC to expand the physician’s choices in quality CME-accredited medical television.

AMT, the only medical programming endorsed by the American Medical Association, has teamed up with CNBC in a major move to make the best in medical television easier and more convenient to watch. Now the new AMT offers the physician CME programs Saturday and Sunday from 10 am – 1 pm (ET). AMT also offers entertaining health and lifestyle segments for your patients from 1 pm – 3 pm (ET) Saturday and Sunday. That’s 10 full hours of medical information every weekend.

The new AMT gives you medical news coverage and practice management information with features like “From the Hill,” “Medical Rounds” and “Journal Watch,” “VideoClinic” and “Milestones in Medicine” offer in-depth clinical updates on a variety of topics.

The new AMT, CNBC. Two great resources combining to bring you a new world of quality medical television. Expand your world. Call 1-800-SMART-TV to find out where you can watch AMT on CNBC in your area.
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While every precaution is taken to ensure accuracy, we cannot guarantee against the possibility of an occasional change or omission in the preparation of this index.
Encouragement

This message could be one of encouragement to you and, perhaps, certain of your patients.

Paget's disease of bone — not the rare disease it was once thought to be — is treatable in most cases. The earlier it is detected the more responsive to treatment it is likely to be. And detection can usually be accomplished with a few simple, non-invasive procedures.

Like many primary care physicians, you may feel uncomfortable treating Paget's disease because of little past experience. If so, write or call us for comprehensive, up-to-date information about the disease and its diagnosis and treatment. Alternatively, ask for our extensive referral list of specialists.

You may be able to offer someone a new lease on life. Or at least, encouragement.
IN MANY CHRONIC ARTHRITIS PATIENTS

Expect Success from the #1 Prescribed NSAID*

A proven efficacy and safety profile backed by 16 years of clinical success.

As with other NSAIDs, the most frequent complaints are gastrointestinal, and rare hepatic and renal reactions have been reported.

See brief summary of prescribing nation on adjacent page.

EXPECT SUCCESS FROM
NAPROSYN®
(NAPROXEN) 500 mg tablets

Also available in 375 and 250 mg tablets and in suspension 125 mg/5 mL.


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