Today's hypertensives with new concerns...

The JNC now recommends selective alpha-1-blockers as a first choice!

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.²⁴

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.
DORAZOLAM (dorzolamide mesylate)

**Table of Contents**

- **INDICATIONS AND USAGE**
- **CONTRAINDICATIONS**
- **WARNINGS**
- **PRECAUTIONS**
- **ADVERSE REACTIONS**
- **DOSEAGE AND ADMINISTRATION**
- **DOSE-RESPONSE**

**INDICATIONS AND USAGE**

DORAZOLAM is indicated for the treatment of hypertension.

**CONTRAINDICATIONS**

DORAZOLAM is contraindicated in patients with a known sensitivity to quinolones (e.g., prazosin, tamsulosin).

**WARNINGS**

While hypotension is the most severe adverse effect of DORAZOLAM, other symptoms, such as dizziness, lightheadedness, or vertigo, can occur, especially at the initiation of therapy or at the time of dose increases. These symptoms are common in clinical trials, occurring in up to 20% of all patients treated and causing discontinuation of therapy in about 2%.

In clinical placebo-controlled studies, hypotension was minimized by beginning therapy at 1 mg/day and titrating every two weeks to 2, 4, or 8 mg/day. In patients with a history of cardiovascular disease, intermittent hypotension has been observed in up to 10% of patients receiving doses of 2 mg/day or higher. In one study, patients with a history of cardiovascular disease experienced intermittent hypotension in up to 10% of patients receiving doses of 2 mg/day or higher. In another study, intermittent hypotension occurred in up to 10% of patients receiving doses of 4 mg/day or higher. In one study, intermittent hypotension occurred in up to 10% of patients receiving doses of 8 mg/day or higher. In one study, intermittent hypotension occurred in up to 10% of patients receiving doses of 16 mg/day or higher. In one study, intermittent hypotension occurred in up to 10% of patients receiving doses of 32 mg/day or higher.

**PRECAUTIONS**

1. **Orthostatic Hypotension:**

   Orthostatic hypotension is a common adverse effect of DORAZOLAM, especially in patients who are dehydrated or have a history of cardiovascular disease. Symptoms may include dizziness, lightheadedness, or vertigo, which can occur at any time during treatment and may worsen with dose increases. These symptoms are often transient and resolve with continued treatment.

2. **Impaired Liver Function:**

   DORAZOLAM should be administered with caution to patients with evidence of impaired liver function, as the drug is excreted primarily by the liver. Patients with liver disease may require dose adjustments or may be at increased risk for adverse effects.

3. **Lupus Nephropathy:**

   Patients who have or have had lupus nephropathy should be monitored closely during treatment with DORAZOLAM. The risk of lupus nephropathy may be increased in patients with lupus vulgaris, and a history of renal impairment should be considered before initiating treatment.

4. **Skin Appendages:**

   The prevalence rates of skin appendage disorders associated with DORAZOLAM therapy are presented below.

**ADVERSE REACTIONS**

**DOSE-RESPONSE**

DORAZOLAM may be used in combination with other antihypertensive agents to achieve blood pressure control. DORAZOLAM is not recommended for use in patients with severe renal impairment (creatinine clearance <30 mL/min).

**DOSEAGE AND ADMINISTRATION**

DORAZOLAM tablets are available in 1 mg, 2 mg, and 4 mg strengths. These strengths are available as follows:

<table>
<thead>
<tr>
<th>Strength</th>
<th>White, oval tablets with &quot;452&quot; imprinted on one side</th>
<th>White, oval tablets with &quot;453&quot; imprinted on one side</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg</td>
<td>10,000 tablets</td>
<td>10,000 tablets</td>
</tr>
<tr>
<td>2 mg</td>
<td>10,000 tablets</td>
<td>10,000 tablets</td>
</tr>
<tr>
<td>4 mg</td>
<td>10,000 tablets</td>
<td>10,000 tablets</td>
</tr>
</tbody>
</table>

**References**


**TABLE 1**

**Adverse Reactions During Placebo-Controlled Studies**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Placebo (N=100)</th>
<th>DORAZOLAM (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>9%</td>
<td>11%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Palpitations</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Edema</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Palpitation</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Arterial Hypertension</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Peripheral ischemia</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Skin Appendages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>MUSCULOSKELETAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia/Arthritis</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Muscle Weakness</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>CENTRAL &amp; PERIPHERAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headaches</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td>Parosymolgia</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Kinetic Disorders</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Dysphoria</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Muscle Cramps</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**DOSEAGE AND ADMINISTRATION**

The initial dosage of DORAZOLAM for mild to moderate hypertension is 1 mg given once daily. This starting dose is intended to maintain the frequency of nocturnal hypotension and first dose syndrome associated with DORAZOLAM. Postural effects are most likely to occur between 2 and 6 hours after a dose. Therefore, blood pressure measurements should be taken during this period after the first dose and with each increase in dose.

Discontinuing the individual patient's standing blood pressure responses (based on measurements taken at 2 and 4 hours post-dose, standing), dosage may then be increased to 2 mg and thereafter if necessary to 4 mg of 8 mg and 16 mg to achieve the desired reduction in blood pressure. However, since the duration of action does not exceed 4 mg, it is recommended that the last dose during each maximum effect is increased to 4 mg, resulting in the effective dosage of each maximum effect. The last dose during each maximum effect is increased to 4 mg, resulting in the effective dosage of each maximum effect. The last dose during each maximum effect is increased to 4 mg, resulting in the effective dosage of each maximum effect.
FOR YOUR PROTECTION:
The OSHA Regulations on Bloodborne Pathogens

OSHA TRAINING KIT AGAIN AVAILABLE FROM AMERICAN MEDICAL TELEVISION AND THE AMERICAN MEDICAL ASSOCIATION

The regulations on bloodborne pathogens, issued by the Occupational Safety and Health Administration (OSHA) last year, continue to change the way health care facilities cope with occupational hazards to their employees. Educating and training health care workers are key elements. A comprehensive training program produced by American Medical Television in conjunction with the American Medical Association, will help the physician, clinics and hospitals comply with the OSHA requirement to train staff in the material covered under these regulations.

Model Exposure Control Plan - Designed to help any health care facility develop their own written procedures, as required by the OSHA Standard. This simple, easy-to-follow format provides a step-by-step approach for compliance, dramatically reducing the time required to develop these written procedures.

Five Training Manuals - Provide back-up reference for employees, reinforcing material presented on the videocassette.

Available in kit format, For Your Protection: The OSHA Regulations on Bloodborne Pathogens includes everything the practicing physician and his or her staff need to comply with the OSHA regulations on bloodborne pathogens plus the mandatory Hepatitis B Vaccine Declination.

Training materials include:

25-minute VHS Videocassette - Covers relevant portions of the OSHA Standards as they apply to most health care facilities, including the physician's office.

Administrator's Guide - Shows the physician or office administrator how to use the training program. The Guide also includes a copy of the amended OSHA Standards. Learn how to train employees, answer questions, and prepare necessary exposure control plans.

For Your Protection: The OSHA Regulations on Bloodborne Pathogens training kit is the only OSHA kit reviewed for accurate medical and scientific content by the American Medical Association.

Completion of this training program has also been designated by the AMA as a Continuing Medical Education activity, worth 2 credit hours of Category 1 of the Physician Recognition Award of the AMA.

The complete For Your Protection: The OSHA Regulations on Bloodborne Pathogens training kit is available for $195, including S & H ($150 for AMA Members, Hospitals, Institutions, Universities, and Government Offices).

To order call 1-800-398-CNBC.

American Medical Television is produced in conjunction with the American Medical Association.
VERELAN
EXCELLENT TOLERABILITY SIMILAR TO PLACEBO IN A DOUBLE-BLIND STUDY

Incidence of side effects commonly associated with calcium channel blockers

<table>
<thead>
<tr>
<th>Side effect</th>
<th>VERELAN clinical trials* (n=295)</th>
<th>Double-blind, placebo-controlled study* VERELAN (n=81)</th>
<th>Placebo (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>7.4%</td>
<td>9.9%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Headache</td>
<td>5.3%</td>
<td>7.4%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4.2%</td>
<td>2.5%</td>
<td>3.8%</td>
</tr>
<tr>
<td>Edema</td>
<td>1.4%</td>
<td>3.7%</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

*Results of a 4-week, double-blind, placebo-controlled study of patients with essential hypertension. VERELAN 120 mg/day, n = 28; 240 mg/day, n = 27; 480 mg/day, n = 26; placebo, n = 26.

No patients discontinued VERELAN therapy due to constipation, headache, dizziness, or edema

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.
Living in Medicine

Choices
Janice E. Nevin, MD, MPH

Letters to the Editor

Revolution in Practice Management:
A New Kind of Drudgery
David M. Moore, MD

In Reply
Christian N. Ramsey, Jr, MD

Welcome to the Family, More Than 'Referralists'
Maury J. Greenberg, MD, D-ABFP

In Reply
John L. Clowe, MD

Science Advocacy:
A Role for the Family Practitioner
Jerod M. Loeb, PhD

Original Contributions

Does the System of Papanicolaou Test Nomenclature Affect the Rate of Referral for Colposcopy?
A Survey of Family Physicians
Joy Melnikow, MD, MPH; Anne Sierk, MD; Susan Flocke, MA; Claudia A. Peters, MD

Commentary
Cervical Cancer: Screening Issues of Collection Tools and Reporting
Mack T. Ruffin IV, MD, MPH

Cryotherapy Precision: Clinician's Estimate of Cryosurgical Iceball Lateral Spread of Freeze
Daron G. Ferris, MD; Gregory R. Crawley, DVM; Elizabeth G. Baxley, MD; Robin Line, MD; Keith Ellis, MD; Peggy Wagner, PhD

Practice Commentary
Wm. MacMillan Rodney, MD

Copyright 1993 by the American Medical Association. All rights reserved. Reproduction without permission is prohibited.

All articles published, including editorials, letters, and book reviews, represent the opinions of the authors and do not reflect the policy of the American Medical Association, the Editorial Board, or the institution with which the author is affiliated, unless this is clearly specified.
Let us help you with questions regarding your subscriptions to American Medical Association publications. Call 1-800-AMA-2350, FAX 312-464-5831. Our Subscriber Services Center is ready to help you. Just call. Your subscription questions can be answered in minutes.

American Medical Association
Physicians dedicated to the health of America
IN HYPERTENSION—

A BALANCE OF GENTLENESS AND POWER

The recommended starting dosage for Calan SR is 180 mg once daily. Dose titration will be required in some patients to achieve blood pressure control. A lower starting dosage of 120 mg daily may be warranted in some patients, e.g., the elderly, patients with small stature. Dosages above 240 mg daily should be administered in divided doses. Calan SR should be administered with food. Constipation, which is easily managed in most patients, is the most commonly reported side effect of Calan SR.

BRIEF SUMMARY

Contraindications: Severe LV dysfunction (see Warnings), hypotension (systolic blood pressure < 80 mm Hg or cardiac shock), or edema (no poacemat is present), atrial flutter/fibrillation with an accessory bypass tract (e.g., WPW or LGL syndromes), and 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 in patients with any degree of ventricular dysfunction if they are taking a beta-blocker. Milder heart failure with optimal digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal or chronic atrial flutter/fibrillation and an accessory AV pathway (e.g., WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway by blocking the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving IV verapamil (or digitalis). Because of this risk, verapamil is contraindicated in such patients. Also, some patients may develop atrial and 3rd-degree block (0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function in severe hypotension (see about 30% of the normal distribution) or impaired renal function, and patients should be monitored for abnormal prolongation of the QT interval or other signs of overdose. Verapamil may decrease neurohumoral transmission in patients with Duchenne's muscular dystrophy and may potentiate recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-blockers and verapamil may result in additive negative effects on heart rate, antimuscular contraction and/or cardiac contractility, there have been reports of excessive bradycardia 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 dose monitoring. Decreased metoprolol and propranolol clearance may occur when other drugs are administered concomitantly with verapamil. A variable effect has been seen with combination of verapamil and isosorbide. 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 extrarenal clearance of digoxin. The digoxin dose should be reduced when verapamil is given, and the patient's digoxin levels should be monitored.

Dyspnea should not be given within 48 hours before or 24 hours after verapamil administration. Concurrent use of triamterene and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypokalemic cardiomyopathy should be avoided, since significant hypokalemia may result. Concurrent use of lithium and verapamil may result in an increased sensitivity to lithium (irreversibility) with abrupt changes in serum lithium levels, however, it may also occur in a lowering of serum lithium levels. Patients receiving both drugs must be monitored carefully. Verapamil may increase carboxyglucuronides concentrations during combined use. If aminoglycosides may reduce verapamil bioavailability. Rhabdomyolysis may increase verapamil clearance. Verapamil may increase serum levels of cyclosporines. Verapamil may inhibit the clearance and increase the plasma levels of theophylline. Concurrent use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing). Dosage reduction may be required. There was no evidence of a carcinogenic potential of verapamil administered to rats for 2 years. A study in rats did not suggest a tumorigenic potential, and verapamil was non-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.

Adverse Reactions: Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (5.5%), headache (2.3%), edema (1.9%), CHF, pulmonary edema (1.1%), fatigue (1.7%), drowsiness (1.4%), bradycardia (0.5%), 1st-degree AV block (1.2%), 2nd-degree AV block (0.9%), rash (1.2%), flushing (0.6%), elevated liver enzymes, reversible non-contraceptive pruritic rash. The following reactions, reported in 1% or less of patients, occurred under conditions where a causal relationship is uncertain, angioedema, anterior chamber obliterative dissection, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, eczema, hives, bruising, cerebrovascular accident, constipation, urticaria, anemia, muscular cramps, paresthesias, psychiatric symptoms, shock, somnolence, arthritis, and rash, xanithemia, hair loss, hyperkalemia, maculopapular rash. The incidence and severity of adverse effects were not different from those observed in placebo-controlled trials.
In osteoarthritis and rheumatoid arthritis

**what you want** in an NSAID*

Efficacy  
Tolerability  
Once-a-day dosing

*Nonsteroidal anti-inflammatory drug.*
*Usual adult dosage is 1200 mg (two 600-mg caplets) once a day. For osteoarthritis patients of low body weight or with milder disease, an initial dosage of one 600-mg caplet once a day may be appropriate.

† As with all NSAIDs, the most frequently reported adverse reactions were related to the GI tract: nausea (8%) and dyspepsia (8%). In patients treated with DAYPRO, as with other NSAIDs in the long-term, serious GI toxicity such as bleeding, ulceration, and perforation can occur and patients should be selected accordingly.

Please see brief summary of prescribing information on last page of this advertisement.
New Two caplets, once a day *

DAYPRO™
(oxaprozin) 600-mg caplets

☑ Efficacy
From the same chemical class as naproxen and ibuprofen, but with the extended duration of action of piroxicam¹

☑ Tolerability
GI tolerability¹ without a loss of therapeutic efficacy¹

☑ Once-a-day dosing
Usual adult dosage is 1200 mg/day (two 600-mg caplets)*

want in an NSAID
Usual adult dosage is 1200 mg (two 600-mg caplets) once a day.*

Experience with NSAIDs has shown that starting therapy with maximal doses in elderly patients or those with CHF, fatalities or serious cardiovascular or gastrointestinal adverse events is likely to increase the frequency of adverse events and is not recommended.

*For osteoarthritis of patients low body weight or with milder disease, an initial dosage of one 600-mg caplet once a day may be appropriate.

**Brief Summary**

**Contraindications:** Patients with previously demonstrated hypersensitivity to oxaprozin or any of its components or in individuals with the complete or partial syndrome of nasol hypoglossia, angioedema, and bronchial/bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs). Severe and lifethreatening anaphylactoid reactions have been reported in patients receiving NSAIDs, and there have been rare reports of anaphylaxis in patients taking oxaprozin.

**Warnings:** Risk of Gastrin-Testosterone (G-T) ULCERATION, BLEEDING, AND PERFORATION WITH NONSTEROIDAL ANTIRHEUMATIC DRUG THERAPY: Serious G-T toxicity, such as bleeding, ulceration, and perforation, can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Although minor upper GI problems, such as dyspepsia, are common, and usually develop early in therapy, physicians should remain alert for ulceration and bleeding in patients treated chronically with NSAIDs, even in the absence of previous GI tract symptoms. In patients observed in clinical trials for several months to 2 years, symptomatic, endoscopically confirmed ulcers, grade bleeding or perforation, did occur in approximately 1% of patients treated for 3 to 6 months, and in about 2% to 4% of patients treated for 1 year or longer. These occurrences should always be borne in mind, and an awareness of the signs and symptoms of serious GI toxicity and what steps to take if they occur. Physiologic studies suggest that ulceration and bleeding are those with a prior history of serious GI events, alcoholism, smoking, or other factors known to increase the risk of GI toxicity of NSAIDs. Management of significant or unexplained G-T bleeding or to tolerate ulceration or bleeding less well than other individuals, and most spontaneous reports of fatal GI events are in these populations. Studies to date are inconclusive concerning the relative risk of various NSAIDs in causing ulcers. With doses of any NSAID, probably carry a greater risk of these reactions.

**Precautions:** As with other NSAIDs, bronchial elevations of one or more liver tests may occur in up to 15% of patients. These abnormalities may progress to severe liver necrosis with or without the clinical features of hepatic failure, and may be fatal. A transient increase in AST and ALT has been observed in oxaprozin patients both with and without renal impairment. The specific cause of this elevation in liver enzyme is not known. Despite this increase, the frequency of liver enzyme abnormalities is not increased when oxaprozin is taken in combination with other drugs that are known to increase liver enzymes, such as another NSAID or allopurinol.

**Adverse Reactions:** The most frequently reported adverse reactions were related to the GI tract. They were nausea (8%) and dyspepsia (6%).

**Incidence Greater Than 1%:** In trials the following adverse reactions occurred at an incidence greater than 1% and are probably related to treatment. Reactions occurring in 3% to 5% of patients treated with Daypro are indicated by an asterisk (*); those occurring in less than 3% by a vertical bar (|). In addition, reactions which may be minor in severity, but may result in discontinuation of the drug or require discontinuation of the drug and in which the incidence is less than 1% but which have been reported rarely and which may be meaningful in a meaningful clinical setting, are included. The incidence of a certain reaction may be greater than 1% because of the inclusion of mild cases.

**Incidence Less Than 1%:** Include only adverse experiences that have not already been mentioned in greater detail, or that were not considered meaningful. The incidence of certain reactions may be greater than 1% because of the inclusion of mild cases.

**General**

**Dizziness:** Dizziness or lightheadedness may occur when getting out of bed quickly, after sitting or lying down. This is more likely to occur in the elderly. If this occurs, let the body get used to the change in position by standing slowly. If this continues, contact a physician.

**Drug Abuse and Dependency:** Daypro is a non-narcotic drug. Usually reliable animal studies have indicated that Daypro has no known addiction potential in humans.

**Overdosage:** No experience existed either an accidental or intentional overdosage of Daypro in the clinical trials of the drug. Symptoms following acute overdose with other NSAIDs are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric distress. If severe, these symptoms may be controlled by supportive care. GI bleeding and coma have occurred following NSAID overdose. Hypertension, acute renal failure, and respiratory depression are rare. Patients should be managed by symptomatic and supportive means following an overdose. There are no specific antidotes. Gastric decontamination may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose; repeat the usual dose. This should be done in consultation with a physician or other health care professional.

**Supportive Care:** Hemodialysis and peritoneal dialysis are usually not effective in removing oxaprozin from the body but in severe cases, such as severe renal failure or anaphylactic shock, plasma exchange has been used successfully. The drug distributes into the breast milk; therefore, nursing should be discontinued when the patient is on oxaprozin. In other cases, oxaprozin should be avoided during lactation.

**Reference:**

1. Data on file, Searle.

2.98D777BT

Address medical inquiries to: G.D. Searle & Co.
Medical & Scientific Information Department
4901 Searle Parkway
Skokie, IL 60077

Box 5110
Chicago, IL 60680-5110

Searle
A safety profile that works in concert with other antihypertensive agents

In limited controlled trials, no notable change in the nature or frequency of adverse reactions was shown when LOZOL® was combined with other antihypertensives. LOZOL® is well tolerated and does not adversely affect the lipid profile.** 

And unlike Dyazide® or Maxzide, there may be no increase in the risk of hyperkalemia when LOZOL® is used in combination with ACE inhibitors.

Calcium excretion is decreased by diuretics pharmacologically related to indapamide. Serum concentrations of calcium increased only slightly with indapamide in long-term studies of hypertensive patients. Indapamide may decrease serum PTH levels without signs of thyroid dysfunction. Complications of hypercalcemia and hyperparathyroidism have not been seen. Decrease before test of parathyroid function is performed.

Thiazides have exerted or activated systemic lupus erythematosus. Consider this possibility with indapamide.

DRUG INTERACTIONS: LOZOL® may add to or potentiate the action of other antihypertensive drugs. The antihypertensive effect of the drug may be enhanced in the posthypertensive patient. Indapamide may decrease oral responsiveness to nonpeptide angiotensin II receptor blockers, but this does not preclude the use of nonpeptide angiotensin II receptor blockers in mouse and rat lethargy cardiomyopathy studies. There were no significant differences in the incidence of tumors between the indapamide-treated animals and the control groups.

Pregnancy Category B: Drugs cross the placental barrier and appear in cord blood. Indapamide should be used during pregnancy only if clearly needed. This may be associated with miscarriage, stillbirth, and/or low birth weight and/or severe liver disease and/or heart failure. Pregnancy-related and non-pregnancy-related and possibly other adverse effects that have occurred in adults. It is not known whether this drug is excreted in human milk. If used in human milk, it is not known whether this drug is excreted in human milk. In the case of this drug is deemed essential, the patient should stop nursing.

ADVERSE REACTIONS: Most adverse effects have been mild and transient. From Phase III placebo-controlled studies and long-term controlled clinical trials, adverse reactions with ≥ 3% cumulative incidence: headache, dizziness, fatigue, weakness, loss of energy, fatigue, lightheadedness, nasopharyngitis, rash, herpes simplex, vertigo, paresthesia, muscular weakness, pruritus, myalgia, back pain, abdominal pain, abdominal distention, arthralgia, anxiety, chest pain, cough, creatinine increase, creatinine phosphokinase increase, nausea, vomiting, diarrhea, diarrhea, abdominal distention, rash, increased AST, increased ALT, anemia, hyperkalemia, nasopharyngitis, orthostatic hypotension, photophobia, paresthesia, upper respiratory tract infection, urticaria, sweating, muscle weakness, sneezing, tachycardia, tremor, toothache, upper respiratory tract infection, urinary tract infection, and upper respiratory tract infection.

Calcium excretion is decreased by diuretics pharmacologically related to indapamide. Serum concentrations of calcium increased only slightly with indapamide in long-term studies of hypertensive patients. Indapamide may decrease serum PTH levels without signs of thyroid dysfunction. Complications of hypercalcemia and hyperparathyroidism have not been seen. Decrease before test of parathyroid function is performed.

Thiazides have exerted or activated systemic lupus erythematosus. Consider this possibility with indapamide.

References:
ily physicians will play the central role in our country's health care provision system and that ways need to be found to ensure that enough patients will flow to other specialists so as to maintain the financial status quo.

Maury J. Greenberg, MD, D-ABFP Stony Brook, NY


In reply

The study I described by the AMA Council on Long Range Planning and Development in cooperation with the American Academy of Family Physicians identified factors that were likely to influence the future of family practice. The study findings were meant to be descriptive, not prescriptive. The fact is, fewer family physicians are including obstetrics in their practices, as the Council predicted and as was noted at the Academy's annual meeting in San Diego, Calif (American Medical News, November 16, 1992:45). Thirty years ago, the majority of family physicians did some obstetrics; today only 25% to 30% do. This is not to say what should happen, merely what is happening. Liability issues have played a part, as have life-style choices and availability of obstetric training.

My comments citing the importance of the family physician as patient advocate and case manager were not meant to "relegate family physicians to the role of 'referralists.'" My point was just the opposite: that family physicians are uniquely trained and suited to provide broad-based, cost-effective care to their patients, referring to other specialists when medically appropriate. Physician specialty may indeed have an impact on resource utilization, as has been suggested recently. The expertise of family physicians and others in primary care specialties is likely to be a key ingredient in health care cost reform.

Dr Greenberg is certainly correct: the scope of family practice is expanding. I hope this new ARCHIVES will contribute to this expanding knowledge base by helping family physicians keep abreast of emerging technologies, procedures, and issues that affect their practice.

John L. Clowe, MD Chicago, Ill


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.

So sharpen your pencil. Write for the free Consumer Information Catalog. And get reading worth writing for.
**Antianginal activity for at least 12 hours**

In clinical trials, Ismo dosed at 8 AM and 3 PM for a period of 2 weeks demonstrated efficacy for at least 12 hours after the first dose, i.e., 5 hours after the second dose, of each day.¹

**Predictable pharmacokinetic profile**

Ismo is nearly 100% bioavailable. Blood levels following oral dosage are as predictable as those seen with i.V. isosorbide mononitrate administration.²

**Helps get active patients active again**

*The dosing schedule of 20 mg, twice daily, 7 hours apart (with a 17-hour dose-free interval) must be followed carefully.
Ismo is not recommended for use in aborting acute anginal episodes. The most common side effect, headache, may be managed with simple analgesics. As with other long-acting nitrates, Ismo is not recommended in patients with acute myocardial infarction or congestive heart failure.

**References:**

Please see brief summary of prescribing information on adjacent page.
Effective lipid management doesn't have to be tough

PRAVACHOL® (pravastatin sodium) is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate.
Effective lipid management — improves key lipids

Significantly reduces LDL-C. Increases beneficial HDL-C.

<table>
<thead>
<tr>
<th>Mean percentage change from baseline after 8 weeks of treatment with 10 to 40 mg of pravastatin*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
</tr>
<tr>
<td>Total C</td>
</tr>
<tr>
<td>Triglycerides</td>
</tr>
<tr>
<td>HDL-C</td>
</tr>
<tr>
<td>+2 to +12%</td>
</tr>
<tr>
<td>-22 to -34%</td>
</tr>
<tr>
<td>-16 to -25%</td>
</tr>
<tr>
<td>-11 to -24%</td>
</tr>
</tbody>
</table>

*Each arrow represents a range of means derived from a single placebo-controlled study that included 35 patients treated with pravastatin.

Excellent safety/tolerability profile for patients

- Low incidence of side effects
- Discontinuation rate from pravastatin (1.7%) was not statistically different from that of placebo (1.2%)
- Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin

Easy dosing regimen and other patient benefits

- Usual dose: 20 mg once daily at bedtime, with or without food
- PRAVACHOL can be used confidently with many other medications

PRAVACHOL®
pravastatin sodium 20 mg tablets

Bristol-Myers Squibb Company

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the final page of this advertisement.
WARNINGS

and

synthesis

did

bioavailability

zygous

decays and cell membrane. Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and may increase HDL cholesterol levels, it is recommended that patients with hypercholesterolemia be monitored closely for changes in HDL cholesterol levels. Patients with familial hypercholesterolemia have a higher baseline HDL cholesterol level and may show a greater increase in HDL cholesterol levels on pravastatin treatment than patients with primary hypercholesterolemia. Dosage increases in the elderly may be more gradual than in younger patients. 

Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness and to consult their physicians. The use of creatine kinase determinations will assist in making the diagnosis. 

Drug Interactions: Immunosuppressive Drugs, Darbepoetin, Mepolizumab, Ertumax, TBCIMJ, INFAS, PGE3, Fidaxomicin, TRECTherapies. Ablation by the cytochrome P450 system was unaltered by concomitant administration of pravastatin and these compounds. 

In a crossover study involving 18 healthy male subjects given pravastatin and digoxin concurrently for 7 days, the steady state plasma concentration of digoxin decreased by 10% in the pravastatin group as compared to placebo. However, this effect was not dose-dependent because the patients took uncontrolled LDL. 

In patients with stabilized doses of pravastatin for 24 patients with varying degrees 1.3 to minimal (as determined by clinical measurements). No effect was observed on the pharmacokinetics of pravastatin, nor was there any significant change in plasma levels of 3-hydroxy-3-methylglutaryl coenzyme A reductase. Gastrointestinal and Nausea/Anorexia, 

Garlic, Ginseng, 

Nasal/Sinus, 

Abdominal Pain, 

Pain, 

Confusion, 

Urticaria, 

Edema, 

Tachycardia, 

Anxiety, 

Food, 

Muscle

Nausea/Anorexia, 

Abnormalities, 

Neutropenia, 

Rheumatoid Arthritis, 

Infertility, 

Mycologic, 

Urinary/Gastrointestinal, 

Respiratory, 

Body System/Event

Pravastatin (N = 900) 

Placebo (N = 90) 

Placebo (N = 570) 

Placebo (N = 111) 

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 1-year study in rats fed pravastatin at doses of 30, 100, or 400 mg/kg body weight, there was an increased incidence of hepatic lymphomas in males at the highest dose level. However, these findings were not confirmed in adequate doses in seven patients and included those who were sufficiently high to be considered life-threatening. In addition, a significant increase in the number of focal hepatic adenomas in the pravastatin-treated group was observed. However, the clinical relevance of these findings is unknown. 

Necrosis and granulomas have also been reported rarely in postmarketing experience, including cases of pancreatitis, particularly in patients with pre-existing liver, kidney, or cardiac disease. In addition, a significant increase in the number of focal hepatic adenomas in the pravastatin-treated group was observed. However, the clinical relevance of these findings is unknown. 

The possible clinical significance of this finding has not been fully evaluated, and it is unknown whether pravastatin increases the risk of these events in the general population. 

In a small study of 50 healthy volunteers, pravastatin did not produce any adverse effects on felling or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although the effect was not observed in a larger and more lengthy study where 11 (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 100 mg/kg body weight, a transient tubular degeneration (increases in blood glucose levels) were noted. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatogenic degeneration, and germ cell formation in dogs. The clinical significance of these findings is unknown. 

Pregnancy: Pregnancy Category C: See CONTRAINDICATIONS. 

It is not known whether pravastatin is teratogenic in rats at doses up to 1000 mg/day or on rats at doses of up to 50 mg/kg/day. These doses resulted in 20% (9/45) of the rats (for the male rats). 

The clinical relevance of these findings is not known. However, a drug-related increase in the number of focal hepatic adenomas in the pravastatin-treated group was observed. 

In a controlled study of 20 patients with primary hypercholesterolemia, pravastatin was administered orally at doses of 10, 20, or 30 mg daily for up to 3 months. 

ADVERSE REACTIONS 

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4 month-long placebo-controlled trials, 17% of pravastatin-treated patients and 12% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug; the difference was not statistically significant. 

In placebo-controlled trials, a statistically significant increase in serum transaminase values was observed and non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events was approximately 35% and no individual event occurred in over 1% of patients. 

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of patients in the pravastatin group were edema, nausea, flatulence, diarrhea, rectal bleeding, and increased cholesterol and triglyceride levels. The percentage of patients in whom these medical events were believed to be related or possibly related to the drug were 1.9%, 4.4%, 2.0%, 0.7%, 1.7%, and 0.2%, respectively. 

The following end points were evaluated in the trials: 

The following end points were evaluated in the trials: 

Neurological dysfunction of certain cranial nerves (including alteration of taste, impairment of extraocular movements, lagophthalmos, facial asymmetry, dysarthria, and paresis), 

Hypersensitivity Reactions: An apparent hypersensitivity to pravastatin has been reported which includes one or more of the following features: anaphylaxis, angioedema, lipoautonomous like syndrome, panniculitis, myositis, arthralgia, arthralgia, rash, angioedema, maculopapular rash, and edema. 

Neurological, 

Hypersensitivity, 

Skin, 

Musculoskeletal, 

Digestive, 

Respiratory, 

Cardiovascular, 

CNS, Other.

CNS, Other. 

However, the clinical relevance of these findings is not known. However, a drug-related increase in the number of focal hepatic adenomas in the pravastatin-treated group was observed. 

In a controlled study of 20 patients with primary hypercholesterolemia, pravastatin was administered orally at doses of 10, 20, or 30 mg daily for up to 3 months. 

In placebo-controlled trials, a statistically significant increase in serum transaminase values was observed and non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events was approximately 35% and no individual event occurred in over 1% of patients. 

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of patients in the pravastatin group were edema, nausea, flatulence, diarrhea, rectal bleeding, and increased cholesterol and triglyceride levels. The percentage of patients in whom these medical events were believed to be related or possibly related to the drug were 1.9%, 4.4%, 2.0%, 0.7%, 1.7%, and 0.2%, respectively. 

The following end points were evaluated in the trials: 

The following end points were evaluated in the trials: 

Neurological dysfunction of certain cranial nerves (including alteration of taste, impairment of extraocular movements, lagophthalmos, facial asymmetry, dysarthria, and paresis), 

Hypersensitivity Reactions: An apparent hypersensitivity to pravastatin has been reported which includes one or more of the following features: anaphylaxis, angioedema, lipoautonomous like syndrome, panniculitis, myositis, arthralgia, arthralgia, rash, angioedema, maculopapular rash, and edema. 

Neurological, 

Hypersensitivity, 

Skin, 

Musculoskeletal, 

Digestive, 

Respiratory, 

Cardiovascular, 

CNS, Other. 

CNS, Other. 

However, the clinical relevance of these findings is not known. However, a drug-related increase in the number of focal hepatic adenomas in the pravastatin-treated group was observed. 

In a controlled study of 20 patients with primary hypercholesterolemia, pravastatin was administered orally at doses of 10, 20, or 30 mg daily for up to 3 months. 

In placebo-controlled trials, a statistically significant increase in serum transaminase values was observed and non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events was approximately 35% and no individual event occurred in over 1% of patients. 

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of patients in the pravastatin group were edema, nausea, flatulence, diarrhea, rectal bleeding, and increased cholesterol and triglyceride levels. The percentage of patients in whom these medical events were believed to be related or possibly related to the drug were 1.9%, 4.4%, 2.0%, 0.7%, 1.7%, and 0.2%, respectively. 

The following end points were evaluated in the trials: 

The following end points were evaluated in the trials: 

Neurological dysfunction of certain cranial nerves (including alteration of taste, impairment of extraocular movements, lagophthalmos, facial asymmetry, dysarthria, and paresis), 

Hypersensitivity Reactions: An apparent hypersensitivity to pravastatin has been reported which includes one or more of the following features: anaphylaxis, angioedema, lipoautonomous like syndrome, panniculitis, myositis, arthralgia, arthralgia, rash, angioedema, maculopapular rash, and edema. 

Neurological, 

Hypersensitivity, 

Skin, 

Musculoskeletal, 

Digestive, 

Respiratory, 

Cardiovascular, 

CNS, Other.
Now, for allergic rhinitis...

ONCE DAILY FOR RELIEF

Once daily for convenience

Once daily for comfort

Once daily for unsurpassed safety

ONCE DAILY Nasacort® Nasal Inhaler

(triamcinolone acetonide)

Turns patient complaints...Into patient compliance

Please see brief summary of prescribing information on adjacent page.
ONCE DAILY FOR RELIEF

ONCE DAILY
Nasal Inhaler
(triamcinolone acetonide)

Turns patient complaints...into patient compliance

For Intranasal Use Only
Shake Well Before Using

BRIEF SUMMARY

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

WARNINGS: The replacement of a systemic corticosteroid with a topical corticoid can be accompanied by signs of adrenal insufficiency and, in addition, some patients may experience exacerbations of withdrawal, e.g., joint and/or muscular pain, lability, and depression. Patients previously treated for prolonged periods with systemic corticosteroids and transferred to topical corticoids should be carefully monitored for acute adrenal insufficiency in response to stress. In these 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 condition.

Children who are on immunosuppressant drugs are more susceptible to infections than healthy children. Chickens and measles, for example, can have a more serious or even fatal course in children immunosuppressed with corticosteroids. In such children, or in adults who have not had these diseases, particular care should be taken to avoid exposure. If exposed, therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG) will, if indicated, may be indicated. If chickenpox develops, treatment with antiviral agents may be considered.

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 discontinuation of treatment with Nasacort Nasal Inhaler.

Triamcinolone acetonide administered intranasally has been shown to be absorbed into the systemic circulation in humans. Patients with active shiners showed absorption similar to that found in normal subjects. Nasacort at 40 mcg/day for 42 days did not measurably affect adrenal response to a six hour corticotropin test. In the same study, prednisolone 10 mg/day significantly reduced adrenal response to ACTH over the same period (see CLINICAL TRAILS section).

Nasacort Nasal Inhaler should be used with caution, if at all, in patents with active or quiescent tuberculosis, infections of the respiratory tract, in patients with untreated fungal, bacterial, or systemic viral infections or ocular herpetic simplex. Because of the inhibitory effect of corticosteroids on wound healing in patients who have experienced recent nasal septum, ears, 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.

Information for Patients: Patients being treated with Nasacort Nasal Inhaler should receive the following information and instructions.

Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice.

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 systemic 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 occurs only rarely, with this product. The patient should contact the physician if they 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 disposed of after 1000 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 15 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 mcg/m²/kg/day (240 mcg/m²/day). However, a few female rats which received maternal-toxic doses of 8 or 15 mcg/kg/day (60 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 maternal-toxic doses (25.6 - 150 mcg/m²/kg/day or 20 - 110 mcg/m²/day, as calculated on a surface area basis). Reproductive performance of female rats and effects on fetuses and offspring were comparable between groups that received placebo and non-toxic or marginally toxic doses (0.3 and 1.0 mcg/kg/day or 3.8 mcg/m²/kg/day and 7.0 mcg/m²/kg/day).

Pregnancy Category C. Like other corticosteroids, triamcinolone acetonide has been shown to be teratogenic in rats and rabbits. Teratogenic effects, which occurred in both species at doses of 0.03, 0.06, and 0.36 mg/kg/day (approximately 0.25, 0.5 and 3.0 mcg/m²/kg/day in the rat and 330, 640 and 1260 mcg/m²/kg/day in the rabbit, as calculated on a surface area basis), included a low incidence of cleft palate and/or internal hydrocephaly and axial skeletal defects. Teratogenic effects, including CNS and ocular malformations, have also been observed in human premature newborns and infants at dosages of 0.2 and 1.0 mcg/m²/kg/day (approximately 6.7 mcg/m²/kg-day). The doses of 0.03, 0.06, 0.09, and 0.36 mg/kg/day used in these toxicology studies are approximately 12.8, 25.5, 38.1, and 317.5 times the minimum recommended dose of 112 mg of Nasacort per day and 3.2, 6, 12.7, and 80 times the maximum recommended dose of 440 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 fetotoxic 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 corticosteroids since their introduction in pharmacologic as opposed to therapeutic doses suggests that such systemic effects from corticosteroids 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: Hypocalcemia may occur in infants born of mothers receiving corticosteroids during pregnancy who should be closely 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, patients with higher doses over prolonged periods. However, a child who already 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 nasal. These patients were treated for an average of 48 days (range 1 to 117 days). The 145 patients enrolled in uncontrolled studies received treatment from 1 to 365 days (average 330 days).

The most prevalent adverse experience was headache, being reported by approximately 18% of the patients who received triamcinolone nasal. Nasal irritation was reported by 2.8% of the patients receiving Nasacort. Other nasal/sinusoidal side effects were reported by fewer than 0.1% of the patients who received Nasacort and included dry mucous membranes, naso-anus 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 reactions.

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).

OVERDOSE: Acute overdose with this dosage forms 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 cause systemic adverse effects if the nasal application of the 15 mg of triamcinolone acetonide was administered at once.

Caution: Federal (U.S.) law prohibits dispensing without prescription.

Please see product circular for full prescribing information.


Marketed by:

RHÔNE-POULENC RORER
RHÔNE-POULENC RORER PHARMACEUTICALS INC.
5000 MORELAND AVENUE
COLOGNEVILLE, PA 19026

NA9X193X0A 1/93 1993 Rhone-Poulenc Rorer Pharmaceuticals Inc. Printed in U.S.A.
FOR CHRONIC ARTHRITIS

EXPECT A REDUCTION
IN JOINT PAIN
AND TENDERNESS

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 275 and 250 mg tablets and in suspension 125 mg/5 mL.

© 1992 Syntex Puerto Rico, Inc. NP93017
"Shahajoi!" in Bangladesh. "Erdul!" in Ethiopia. "Ayndume!" in Central America. In any language, when the world cries "Help!" CARE is there. Please Be there for CARE.

1-800-242-GIVE
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 58,000,000 prescriptions written for once-daily verapamil SR over the past 6 years.

ONCE-DAILY ISOPTIN SR (verapamil HCl)

180/240 mg Sustained-Release Tablets

*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.

Please see back for brief summary of prescribing information.
ONCE-DAILY ISOPTIN SR (verapamil HCl) Sustained-Release Tablets

Unsurpassed dosage flexibility

Brief Summary of Prescribing Information

CONTRAINDICATIONS: 1) Severe left ventricular dysfunction (see WARNINGS). 2) Hypotension (less than 90 mm Hg systolic) 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., Wolf-Parkinson-White, Lown-Ganong-Levine syndromes). 6) Patients with known hypertension and verapamil hydrochloride.

WARNINGS: Heart Failure: ISOPTIN should be avoided in patients with severe left ventricular dysfunction. Patients with mild 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 concurrent elevations in alkaline phosphatase and bilirubin have been reported. Periodic monitoring of liver function in patients receiving verapamil is therefore prudent. Accessory Bypass Tract (Wolff-Parkinson-White): Patients with paroxysmal or chronic atrial flutter or atrial fibrillation and a coexisting accessory AV pathway may develop marked increase in conduction across the accessory pathway producing a very 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 CONTRAINDICATIONS). Treatment is usually D.C. cardioversion. Anticonvulsant 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, if necessary, discontinuation of verapamil. HCl. Patients with Hypertrophic Cardiomyopathy (HOCM): Although verapamil has been used in the therapy of patients with HOCM, severe myocardial 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 30% of the usual dose and the patient closely monitored. In patients with impaired renal function verapamil should be administered cautiously and the patient monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see OVERDOSE). Use in Patients with Attenuated (Decreased) Neuronal Transmission: Verapamil decreases neuronal transmission and may prolong recovery from neuromuscular blocking agents. In patients with attenuated neuronal transmission lower doses of verapamil may be warranted.

Drug Interactions: Beta Blockers: Concomitant use of ISOPTIN and oral beta-adrenergic blocking agents may result in additive negative effects on heart rate, anticonvulsive and/or cardiac contractility. Excessive bradycardia and AV block has been reported. The combination should be used only with caution and close monitoring.

Digitalis: Digitalis use with verapamil in digitoxin 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 digitotoxicity. 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.

Antidiabetic Agents: DIABETES 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. Burendine: In patients with hypertrophic cardiomyopathy (HOCM), concomitant use of verapamil and quinidine may result in significant hypotension.

Other: Nitrites: The pharmacologic profile of verapamil and nitrites 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: Pharmacologic 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. Rifampicin: Therapy with rifampicin 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 action 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 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 12 years have not been established.

ADVERSE REACTIONS: Constipation 7.9%, dizziness 3.3%, nausea 2.7%, hyperglycemia 2.5%, headache 2.2%, edema 1.9%, CHF-pulmonary edema 1.8%, fatigue 1.7%, dizziness 1.4%, bradycardia 1.4%, and vomiting 0.9%. Rash, flushing 0.5% and elevated liver enzymes (see WARNINGS). The following reactions, reported in less than 1.0% of patients, occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain. They are mentioned to alert the physician to a possible relationship: anemia, confusion, ataxia, hypotension, syncope, dizziness, tachycardia, arrhythmia, nausea, vomiting, diarrhea, dyspnea, bradycardia, atrioventricular block, chest pain, claudication, confusion, diarrhea, dry mouth, cough, eczema, oral or respiratory, disorders, dizziness, drowsiness, sweating, syncope, urticaria.

Treatment of Acute Cardiovascular Adverse Reactions: Whenever severe hypotension or complete AV block occur following oral administration of verapamil, the appropriate emergency measures should be applied immediately e.g., intravenous administration of epinephrine-HC, levaterolol, nitroglycerin, atropine, isoproterenol, dopamine (all in the usual doses), or calcium gluconate (10% solution). If further support is necessary, inotropic agents (doxaprine 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.

OVERDOSE: 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 deliberate overdose with verapamil. Clinically significant hypotensive reactions or fixed high degree AV block should be treated with vasopressor agents or cardopacemaking, respectively. Asystole should be handled by the usual measures including cardopulmonary resuscitation.

DOSAGE AND ADMINISTRATION: Basic Hypertension: The dose of ISOPTIN SR should be individualized by titration and the drug should be administered with food. Initial 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 vaspasmolators e.g., the elderly or small people, etc. Upward titration should be based on therapeutic effect and safely evaluated 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 within 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.

Printed in U.S.A.

27672-86
2003 Knoll Pharmaceutical Company
30 North Jefferson Road
Whippany, New Jersey 07101

@ 2002, Knoll Pharmaceutical Company
I2065-12-92 Printed in USA
SUPRAX
Maintains Inhibitory Concentrations Above MIC_{90} for Virtually 24 Hours*

For β-lactam antibiotics... In order to achieve an optimal antibacterial effect, antibiotic concentrations must exceed the MIC_{90} for the majority of the dosing interval.¹

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

Cefixime 400 mg q24h serum levels v MIC_{90} for respiratory pathogens²,³:

*MIC_{90} values from Jones and Barry.²
COVERS DAY AND NIGHT

In Bronchitis: Excellent Clinical Results

- In a surveillance study of over 9600 patients, SUPRAX cured or improved 95% of patients.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Bronchitis</td>
<td>95%</td>
</tr>
<tr>
<td>Cured or improved (n=8,127)</td>
<td></td>
</tr>
<tr>
<td>Acute Exacerbations of Chronic Bronchitis</td>
<td>95%</td>
</tr>
<tr>
<td>Cured or improved (n=1,322)</td>
<td></td>
</tr>
</tbody>
</table>

1 Due to indicated susceptible organisms.

ONCE-A-DAY
SUPRAX
cefixime/Lederle
400 mg Tablets
24 HOUR POWER

SUPRAX is administered as a single dose, once a day, or if preferred, in equally divided doses twice a day.
Please see brief summary of Prescribing Information on adjacent page.

7508-2
**ONCE-A-DAY SUPRAX**

**cefixime/Lederle**

400 mg Tablets

**24 HOUR POWER**

**REFERENCES**


**BRIEF SUMMARY**

**SUPRAX® cefixime**

Please see package insert for full Prescribing Information.

**INDICATIONS AND USAGE**

Oral use in the treatment of: bacterial pneumonia (Streptococcus pneumoniae), uncomplicated urinary tract infections caused by Escherichia coli or Proteus mirabilis, and gonococcal urethritis and cervicitis. These conditions are not always predictable and therefore a careful medical judgment must be exercised when choosing antibiotics for prophylactic or empirical purposes.

**CLINICAL STUDIES**

In clinical trials of cefixime in the treatment of S. pneumoniae infections, 1 or fewer patients had adverse reactions or reports of complications related to use of the drug. There have been no adverse reports of complications related to use of the drug in the following trials: Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome, Middle East Respiratory Syndrome.

**ADVERSE REACTIONS**

TENORMIN® (atenolol) is a beta-adrenergic blocking agent and is indicated in the management of hypertension. It may be used alone or in combination with other antihypertensive agents, particularly with a thiazide diuretic.

Acute Myocardial Infarction: TENORMIN® is indicated in the management of hypertensive and normotensive patients with acute myocardial infarction. (See DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS.) In general, there is no need for treating patients with the usual dosages of beta blockers. In studies of TENORMIN® in this setting, a mortality rate advantage was not observed. A mortality rate disadvantage was observed, however, in a small number of patients in one study. (See CONTRAINDICATIONS.)

Contraindications: TENORMIN® is contraindicated in those with bradycardia, heart block, heart block of degree 3, carotid sinus syndrome, severe chronic obstructive pulmonary disease, or severe chronic pulmonary disease.

WARNINGS: 
Contraindications: Patients with acute myocardial infarction, cardiac failure which is not promptly and effectively controlled by 80 mg of intravenous furosemide or 100 mg of aminophylline or 40 mg of morphine (see CONTRAINDICATIONS).

In Patients Without a History of Cardiac Failure: Continued depression of the myocardium with beta-blocking agents over a period of time may lead to cardiac failure. The cardiac failure may be reversible if the beta blocker is discontinued. If a patient shows signs of cardiac depression following the use of beta blockers, it may be prudent to discontinue it. In the few patients who have had cardiac failure and who have been treated with inhibitiv therapy, it was recommended that TENORMIN be promptly discontinued, at least temporarily. Persistence of any signs of cardiac depression should prompt consideration of discontinuation of the thiazide diuretic and other agents to determine the extent of cardiac dysfunction, as well as in patients treated for hypertension.

WARNINGS: 
Contraindications: Patients with acute myocardial infarction, cardiac failure which is not promptly and effectively controlled by 80 mg of intravenous furosemide or 100 mg of aminophylline or 40 mg of morphine (see CONTRAINDICATIONS).

In Patients Without a History of Cardiac Failure: Continued depression of the myocardium with beta-blocking agents over a period of time may lead to cardiac failure. The cardiac failure may be reversible if the beta blocker is discontinued. If a patient shows signs of cardiac depression following the use of beta blockers, it may be prudent to discontinue it. In the few patients who have had cardiac failure and who have been treated with inhibitiv therapy, it was recommended that TENORMIN be promptly discontinued, at least temporarily. Persistence of any signs of cardiac depression should prompt consideration of discontinuation of the thiazide diuretic and other agents to determine the extent of cardiac dysfunction, as well as in patients treated for hypertension.

TENORMIN® may be expected to show adverse reactions similar to those observed with other beta blockers. The use of TENORMIN® with other beta blockers requires caution and careful dosage adjustment. The use of TENORMIN® with other beta blockers should be limited to situations in which the use of a single beta blocker is inadequate or contraindicated.

TENORMIN® may cause exacerbation of bronchospasm in patients with known bronchial hyperreactivity. Beta blockers may cause bronchospasm in some patients, particularly those with pre-existing chronic obstructive pulmonary disease. Exacerbation of bronchospasm may be rapidly reversible by discontinuation of the drug. Caution should be exercised against the use of beta blockers in such patients.

Dosage: In patients with normal renal function and normal serum creatinine levels, the maximum recommended daily dose of TENORMIN is 50 mg to 200 mg. In patients with severe renal impairment, the maximum recommended daily dose of TENORMIN is 25 mg. In patients with moderate renal impairment, the maximum recommended daily dose of TENORMIN is 50 mg.

Dosage: In patients with normal renal function and normal serum creatinine levels, the maximum recommended daily dose of TENORMIN is 50 mg to 200 mg. In patients with severe renal impairment, the maximum recommended daily dose of TENORMIN is 25 mg. In patients with moderate renal impairment, the maximum recommended daily dose of TENORMIN is 50 mg.

Dosage: In patients with normal renal function and normal serum creatinine levels, the maximum recommended daily dose of TENORMIN is 50 mg to 200 mg. In patients with severe renal impairment, the maximum recommended daily dose of TENORMIN is 25 mg. In patients with moderate renal impairment, the maximum recommended daily dose of TENORMIN is 50 mg.

Dosage: In patients with normal renal function and normal serum creatinine levels, the maximum recommended daily dose of TENORMIN is 50 mg to 200 mg. In patients with severe renal impairment, the maximum recommended daily dose of TENORMIN is 25 mg. In patients with moderate renal impairment, the maximum recommended daily dose of TENORMIN is 50 mg.

Dosage: In patients with normal renal function and normal serum creatinine levels, the maximum recommended daily dose of TENORMIN is 50 mg to 200 mg. In patients with severe renal impairment, the maximum recommended daily dose of TENORMIN is 25 mg. In patients with moderate renal impairment, the maximum recommended daily dose of TENORMIN is 50 mg.

Dosage: In patients with normal renal function and normal serum creatinine levels, the maximum recommended daily dose of TENORMIN is 50 mg to 200 mg. In patients with severe renal impairment, the maximum recommended daily dose of TENORMIN is 25 mg. In patients with moderate renal impairment, the maximum recommended daily dose of TENORMIN is 50 mg.

Dosage: In patients with normal renal function and normal serum creatinine levels, the maximum recommended daily dose of TENORMIN is 50 mg to 200 mg. In patients with severe renal impairment, the maximum recommended daily dose of TENORMIN is 25 mg. In patients with moderate renal impairment, the maximum recommended daily dose of TENORMIN is 50 mg.
Why Consider Tenormin Before All Other Beta Blockers?

- Convenient, once-daily dosing for all indications
- Effective control of blood pressure and angina
- Cardioprotection—improving survival during and after MI³⁴
- Well-tolerated

I.V. INJECTION/TABLETS

Tenormin (atenolol)

* Good clinical judgment suggests that patients who are dependent on sympathetic stimulation for adequate cardiac output and BP are not good candidates for beta blockade. In addition to patients excluded from the ISIS-1 study, those with borderline BP (ie, systolic < 120, especially if over age 80) are less likely to benefit.


See adjacent page for brief summary of prescribing information.
Announcing
The American Medical Association

Morris Fishbein Fellowship
July 1, 1993 through June 30, 1994

Applications are now being taken for the Morris Fishbein Fellowship in Medical Journalism sponsored by the American Medical Association. Physicians interested in making a substantial commitment to medical journalism are invited to apply for this full-time one-year fellowship program.

Work With JAMA The successful candidate will work with the editorial and production staff of The Journal of the American Medical Association in all facets of editing and publishing a major weekly journal. At the completion of the program, it is expected that the candidate will be proficient in all aspects of manuscript selection, issue makeup, copy editing and styling, art and layout of articles, issue planning and managing, in addition to the many other elements of journal publication. He/she will also be conversant with marketing and advertising procedures.

Publishing The candidate must have proven writing ability at the time of application, for he/she will be required during the course of the year to prepare articles for publication. Although the fellow will work under the supervision of a physician-editor, ability to work independently is a must.

Stipend A stipend of $40,000 will be provided to the successful candidate to cover the 1-year period.

Application Forms For an application blank, please write to: Richard M. Glass, MD, Deputy Editor, Journal of the American Medical Association, 515 North State Street, Chicago, IL 60610.

Deadline For Applying Completed applications should be forwarded as soon as possible and must be received no later than March 1, 1993.

American Medical Association
Physicians dedicated to the health of America
NEW FOR ANGINA

THE ONE

CARDIZEM® CD
(diltiazem HCl) 120-, 180-, 240-, 300-mg Capsules

ONCE A DAY
NEW FOR ANGINA

CARDIZEM® CD
(diltiazem HCl) 120-, 180-, 240-, 300-mg Capsules

PROVEN 24-HOUR CONTROL

ONCE A DAY
IN ANGINA AND HYPERTENSION*

24-hour control through a **unique delivery system** designed specifically for diltiazem†

0-12 hours

12-24 hours

CARDIZEM CD provides 24-hour plasma levels similar to those of Cardizem tablets tid at steady state†

One daily dose provides effective plasma levels†

---

* Cardizem CD is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive medications. Cardizem CD is indicated for the management of chronic stable angina and angina due to coronary artery spasm.

† Patent pending.

Please see brief summary of prescribing information on adjacent page.
NEW FOR ANGINA

CARDIZEM® CD
(diltiazem HCl) 120-, 180-, 240-, 300-mg Capsules

PROVEN 24-HOUR EFFICACY

ONCE A DAY
IN ANGINA

Reduces the frequency of angina attacks — through 24 hours

**Total angina attacks**

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=39)</td>
<td>6.35 ±1.49</td>
<td>4.43 ±1.09</td>
</tr>
<tr>
<td>Cardizem CD 120 mg qd (n=37)</td>
<td>3.78 ±1.09</td>
<td>2.30 ±0.73</td>
</tr>
<tr>
<td>Cardizem CD 360 mg qd (n=40)</td>
<td>4.21 ±0.99</td>
<td>1.33 ±0.41</td>
</tr>
</tbody>
</table>

**On Exertion**

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=39)</td>
<td>3.40 ±0.53</td>
<td>2.78 ±0.54</td>
</tr>
<tr>
<td>Cardizem CD 120 mg qd (n=37)</td>
<td>2.48 ±0.32</td>
<td>1.82 ±0.58</td>
</tr>
<tr>
<td>Cardizem CD 360 mg qd (n=40)</td>
<td>2.73 ±0.71</td>
<td>0.97 ±0.37</td>
</tr>
</tbody>
</table>

* At rest and on exertion.

IN HYPERTENSION

Consistent antihypertensive effect seen throughout 24 hours

- Overall study results (127 patients) show a significant mean change at 24 hours in both diastolic (P=0.0075) and systolic (P=0.0009) blood pressure vs placebo
- Cardizem CD average daily dose 268 mg/day

Unlike some once-a-day antihypertensives, titration to bid dosing is not necessary with Cardizem CD

Please see brief summary of prescribing information on adjacent page.
NEW FOR ANGINA

CARDIZEM® CD
(diltiazem HCl) 120-, 180-, 240-, 300-mg Capsules

EXEMPLARY TOLERABILITY WITH
CONVENIENT DOSING

ONCE
A DAY
IN ANGINA AND HYPERTENSION

Extremely well tolerated

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Cardizem CD n=607</th>
<th>Placebo n=301</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>5.4%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3.0%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>3.3%</td>
<td>1.3%</td>
</tr>
<tr>
<td>AV Block First Degree</td>
<td>3.3%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Edema</td>
<td>2.6%</td>
<td>1.3%</td>
</tr>
<tr>
<td>ECG Abnormality</td>
<td>1.6%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Asthenia</td>
<td>1.8%</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

In clinical trials of Cardizem CD capsules, Cardizem tablets, and Cardizem SR capsules involving over 3200 patients, the most common events (i.e., greater than 1%) were edema (4.6%), headache (4.6%), dizziness (3.5%), asthenia (2.6%), first-degree AV block (2.4%), bradycardia (1.7%), flushing (1.4%), nausea (1.4%), and rash (1.2%).

COMPLIANCE-ENHANCING ONCE-DAILY DOSING

120-mg capsules
180-mg capsules
240-mg capsules
300-mg capsules

For angina or hypertensive patients, a recommended starting dose:

- One 180-mg capsule daily
- If necessary, titrate to optimum response

LOWER PRICE

Based on average wholesale prices using equivalent mg/day doses:

- 35% lower cost than Cardizem® (diltiazem HCl) tablets for angina
  — Cardizem tablets are available as 30, 60, 90, and 120 mg
- 25% lower cost than Cardizem® SR (diltiazem HCl) capsules for hypertension
  — Cardizem SR capsules are available as 60, 90, and 120 mg

Please see brief summary of prescribing information on adjacent page.
1. Fungicidal action

- Naftin® is fungicidal, not just fungistatic, to dermatophytes at low concentrations.¹
- Imidazoles (Spectazole®, Nizoral®, Lotrimin® and Lotrisone®*) are fungistatic at low concentrations.

3. Broad spectrum coverage

- Naftin® is effective against the dermatophytes which are associated with the majority of tinea infections.

Recommend Broad Spectrum Naftin® (naftifine hydrochloride) for the everyday treatment of tinea pedis, tinea cruris.

For a copy of "Diagnosis and Treatment of Fungal Infections" please see adjacent page for brief summary of press releases.

*In vitro data, clinical significance unknown. A low incidence of irritation and
2. Rapid symptomatic relief

- Even without a steroid, Naftin® Cream is as effective as Lotrisone® at relieving tinea-related pruritus and erythema.¹
- In comparative studies, Naftin® Cream-treated patients showed a marked decrease in scaling at week one and fissuring at week two compared to Spectazole®-treated patients.²

Naftin® (naftifine hydrochloride) 1% Cream and Gel is and tinea corporis.

Call 1-800-934-3169.

Dryness was observed in clinical trials with Naftin® Cream.

For more information, call 1-800-934-3169.
NAFTIN®
(naftine hydrochloride) 1%
Cream & Gel

INDICATIONS AND USAGE: Naftin® Cream, 1% is indicated for topical application in the treatment of tinea pedis, tinea cruris and tinea corporis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum. Naftin® Gel, 1% is indicated for the topical treatment of tinea pedis, tinea cruris and tinea corporis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans* and Epidermophyton floccosum. "Efficacy for this organism in this organ system was studied in fewer than ten infections. CONTRAINDICATIONS: Naftin® Cream and Gel, 1% is contraindicated in individuals who have shown hypersensitivity to any of its components. WARNING: Naftin® Cream and Gel, 1% is for topical use only and not for ophthalmic use. PRECAUTIONS: General: Naftin® Cream and Gel, 1% is for external use only. If irritation or sensitivity develops with the use of Naftin® Cream and Gel, 1%, treatment should be discontinued and appropriate therapy instituted. Diagnosis of the disease should be confirmed either by direct microscopic examination of a smear of infected tissue or a solution of potassium hydroxide or by culture on an appropriate medium. Information for patients: The patient should be told: 1. Avoid the use of occlusive dressing or wrapping unless otherwise directed by the physician. 2. Keep Naftin® Cream and Gel, 1% away from the eyes, nose, mouth and other mucous membranes. Carcinogenesis, mutagenesis, impairment of fertility: Long-term animal studies to evaluate the carcinogenic potential of Naftin® Cream and Gel, 1% have not been performed. In vitro and animal studies have not demonstrated any mutagenic effect or effect on fertility. Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproductive studies have been performed in rats and rabbits (via oral administration) at doses 150 times or more the topical human dose and have revealed no evidence of impaired fertility or harm to the fetus due to naftine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Nursing mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Naftin® Cream and Gel, 1% is administered to a nursing woman. Pediatric use: Safety and effectiveness in children have not been established. ADVERSE REACTIONS: During clinical trials with Naftin® Cream, 1%, the incidence of adverse reactions was as follows: burning/tinging (6%), dryness (3%), erythema (2%), itching (2%), local irritation (2%). During clinical trials with Naftin® Gel, 1%, the incidence of adverse reactions was as follows: burning/tinging (5%), itching (1%), erythema (0.5%), rash (0.5%), skin tenderness (0.5%).

REFERENCES

Spectazole® is a registered trademark of Ortho Pharmaceutical. Nitrazol® is a registered trademark of Janssen Pharmaceuticals Inc. Lotrinos® and Lotrinos® are registered trademarks of Schering Corp.

ALLERGAN Herbert
Skin Care Division of Allergan, Inc., Irvine, CA 92715
©1993 Allergan, Inc.
Acute Pain Relief, Delivered in Minutes

Brief Summary

INDICATIONS

STADOL NS (butorphanol tartrate) Nasal Spray is indicated for the management of pain when the use of an opioid analgesic is appropriate.

CONTRAINDICATIONS

STADOL NS is contraindicated in patients hypersensitive to butorphanol tartrate or the preservative benzalkonium chloride.

WARNINGS

Pregnancy and Lactation

Because of its opioid antagonist properties, butorphanol is not recommended for use in pregnant women or breastfeeding mothers. In animal studies, butorphanol has been shown to cause fetal resorptions, fetal malformations, and fetal deaths. It is not known whether butorphanol presents a risk to the fetus in humans.

Geriatric Use

Initially 1 mg dose of STADOL NS (butorphanol tartrate) Nasal Spray should generally be used in geriatric patients and 90-120 minutes should elapse before deciding whether a second 1 mg dose is needed.

ADVERSE REACTIONS

A total of 5464 patients were studied in butorphanol clinical trials. Approximately half received STADOL Injectable with the remainder receiving STADOL NS. In reality in all cases the type and incidence of side effects with butorphanol (by any route) were those commonly observed with opioid analgesics. The adverse experiences described below are based on data from short-term and long-term clinical trials in patients receiving butorphanol by any route and from post-marketing experience with STADOL Injectable. There has been no attempt to correct for placebo effect or to confound the frequencies reported by placebo treated patients in controlled trials.

Reactions

The most frequently reported adverse experiences among all clinical trials with STADOL Injectable and STADOL NS were confusion (4%), dizziness (10%), nausea and vomiting (9%), and in long-term trials with STADOL NS only, nasal congestion (13%) and in severe nausea (11%) were frequently reported.

The following adverse experiences were reported at a frequency of 1% or greater and were considered to be probably related to the use of butorphanol:

BODY AS A WHOLE: headache, asthenia, sensation of heat
CARDIOVASCULAR: palpitations
NERVOUS SYSTEM: dizziness, nervousness, weakness and dizziness
RESPIRATORY: rhinitis, cough, dyspnea, epistaxis, nasal congestion, nasal irritation, pharyngitis, laryngitis
SKIN AND APPENDAGES: sweats, palpitations, pruritus

SPECIAL SENSATIONS: blurred vision, ear pain, tinnitus, unpleasant taste (also seen in short-term trials with STADOL NS)

(Reactions occurring with a frequency of 3% or more are listed in an asterisk. * Reactions reported predominantly from long-term trials with STADOL NS are CAPITALIZED)

The following adverse experiences were reported with a frequency of less than 1%, in clinical trials or from post-marketing experience and were considered to be probably related to the use of butorphanol:

CARDIOVASCULAR: hypotension
NERVOUS SYSTEM: abnormal dreams, agitation, drug dependence, dysphoria, hallucinations, paresthesias, tremor
SKIN AND APPENDAGES: rash
URINARY: impotence

(Reactions reported only from post-marketing experience are italicized)

DRUG ABUSE AND DEPENDENCE

Although the mixed agonist-antagonist opioid analgesics, as a class, have lower abuse potential than morphine, all such drugs can be and have been reported to be abused. Chronic use of STADOL Injectable has been reported to result in mild withdrawal symptoms, and reports of overuse and self-reporting of drug dependency have been received.

Among 181 patients who used STADOL NS for more than 1 month, 4% had behavioral symptoms suggestive of possible abuse. Approximately 1% of these patients reported significant overall symptoms. Patients who had symptoms suggestive of opioid withdrawal occurred in 2 patients who stopped the drug abruptly after using 16 mg a day or more for longer than 3 months.

Special care should be exercised in administering butorphanol to emotionally unstable patients and to those with a history of drug misuse. When long-term therapy is necessary, such patients should be closely supervised.

OVERDOSE

Clinical manifestations of overdose are those of opioid drugs, the most serious of which are hypotension, cardiovascular insufficiency, hypothermia, and overdose. Overdose can occur due to accidental or intentional misuse of butorphanol, especially in young children who may gain access to the drug in the home.

Treatment

If the patient is breathing normally, immediate efforts to maintain or improve respiration should be given. The use of a specific opioid antagonist such as naloxone should be considered. As the duration of butorphanol action usually exceeds the duration of action of naloxone, repeated dosing with naloxone may be required.

DOSAGE AND ADMINISTRATION

Factors to be considered in determining the dose are age, body weight, physical condition, use of other drugs, type of anesthesia to be used, and surgical procedure involved. Use in the elderly, children with hepatic or renal disease, or in patients requiring extra caution (see PRECAUTIONS). The following doses are for patients who do not have impaired hepatic or renal function and who are not on CNS active drugs.

The usual recommended dose for initial nasal administration is 1 mg (1 spray in one nostril). Adherence to this dose reduces the incidence of dryness and dizziness. The adequate pain relief is not achieved within 60-90 minutes, an additional 1 mg dose may be given.

The initial two dose sequence outlined above may be repeated in 3-4 hours as needed.

The duration of the pain, an initial dose of 2 mg (1 spray in each nostril) may be used in patients who will be able to return in 3-4 hours in the event dryness or dizziness occurs. In such patients single additional 2 mg doses should not be given for more than 3-4 hours.

Safety and Handling

STADOL NS is an auto-injection system with increased risk of exposure to health care workers.

In the printing process, a certain amount of butorphanol may be aerosolized, therefore the pump sprayer should be aimed away from the patient or other people or animals.

The unit should be disassembled by removing the drug, rinsing the bottle, and placing the parts in a waste container.

How Supplied

STADOL NS is supplied in a child-resistant prescription vial containing a metered-dose spray pump and protective clip with dust cover, a bottle of nasal saline solution, and a patient instruction booklet. On average, one bottle will deliver 14-15 doses if the dispensing is necessary.

NDC 0977-5580-41 mL of butorphanol tartrate 1 mg/mL 2.5-ml bottle.

Storage Conditions

Store below 60° F (20° C). Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Caution: Federal law prohibits dispensing without prescription.
Acute pain relief... from a nasal spray

A Potent Analgesic
- Synthetically derived opioid analgesic with sedative properties
- Efficacy comparable to IM meperidine at equipotent doses\(^1\)
- Somnolence (43\%) is the most frequently reported side effect\(^6\)

In a Convenient Nasal Spray
- The only nasal spray analgesic
- Well suited for outpatient management of acute pain with appropriate medical instruction
- Not a federally controlled substance

Effective in Acute Pain
- Demonstrated efficacy in relief of acute pain following invasive surgical procedures\(^1\)
- Also proven effective in the relief of acute migraine pain\(^2\)
- Onset of pain relief within 15 minutes\(^1,2\)

STADOL\textsuperscript{NS}\textsuperscript{TM} (butorphanol tartrate) Nasal Spray
Acute Pain Relief, Delivered in Minutes

\(^{3}\) STADOL\textsuperscript{NS}\textsuperscript{TM} package insert.

Please see brief summary of prescribing information on following page.
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, dyspepsia and abdominal pain

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.
How do you stay current when the knowledge base of medicine doubles every few years?

Medicine advances at an amazing pace, yet you can remain current through a wealth of CME opportunities offered to you.

To keep abreast of these programs, conferences, workshops and accreditation activities, order the new Continuing Medical Education Directory.

This complete reference, just published by the American Association of Medical Physicians (AMA), contains information not available anywhere else. It pulls together all the information you need to fulfill your CME obligations, including:

- CME requirements of state licensing authorities, state and specialty societies, and the AMA's Physician's Recognition Award.
- State and national society meeting dates.
- Easy-to-use listings of self-assessment and personalized CME programs.

The Continuing Medical Education Directory serves as a unique reference for CME planners, too.

To order your copy, call 800 621-8335 (OP412492DS). The price is only $36 for members of the AMA and $45 for nonmembers.
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

15 years of proven clinical experience

- Effective central and peripheral pain relief.
- Excellent patient acceptance—nausea, sedation and constipation have rarely been reported.¹
- Four to six hours of extra strength pain relief from a single dose.
- The heritage of VICODIN® — over one billion doses prescribed.²
- The 8th most frequently prescribed medication in America.²

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

Extra strength pain relief you can phone in.

¹ Data on file, Knoll Pharmaceutical Company
² Standard industry new prescription audit.
*(hydrocodone bitartrate 5mg [Warning: May be habit forming] and acetaminophen 500 mg)

©1992, Knoll Pharmaceutical Company
V3087/10-92 Printed in U.S.A.
Maintain control of your patient’s pain 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 may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries. Acute Abdominal Conditions: The administration of narcotics may mask the diagnosis or clinical course of patients with acute abdominal conditions. PRECAUTIONS: Special Risk Patients: VICODIN/VICODIN ES Tablets should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, prostatic hypertrophy, and with patients receiving other narcotic analgesics, antihypertensives, antianxiety agents, or other CNS depressants (including alcohol) concomitantly with VICODIN/VICODIN ES Tablets may exhibit an additive CNS depression. The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone. The concurrent use of anticholinergics with hydrocodone may produce paralytic ileus. Usage in Pregnancy: Teratogenic Effects: Pregnancy Category C. Hydrocodone has been shown to be teratogenic in hamsters when given in doses 7 times the human dose. There are no adequate and well-controlled studies in pregnant women. VICODIN/VICODIN ES Tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Nonteratogenic Effects: Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stooling, sweating, yawning, vomiting, and fever. Labor and Delivery: Administration of VICODIN/VICODIN ES Tablets to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used. Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from VICODIN/VICODIN ES Tablets, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Pediatric Use: Safety and effectiveness in children have not been established. ADVERSE REACTIONS: The most frequently observed adverse reactions include drowsiness, dizziness, dizziness, sedation, nausea and vomiting. These adverse effects seem to be more prominent in ambulatory than in nonambulatory patients and some of these adverse reactions may be alleviated if the patient lies down. Other adverse reactions include: Central Nervous System: Drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, psychic dependence and mood changes. Gastrointestinal System: The anticholinergic properties are useful in suppressing the nausea and vomiting which may occur (see above); however, some anticholinergic derivatives seem to be antianalgesic and to increase the amount of narcotic required to produce pain relief, while other phenothiazines increase the amount of narcotic required to produce a given level of analgesia. Prolonged administration of VICODIN/VICODIN ES Tablets may produce constipation. Genitourinary System: Urinary spasm, spasm of vesical sphincters and urinary retention have been reported. Respiratory Depression: Hydrocodone bitartrate may produce dose-related respiratory depression by acting directly on the brainstem respiratory center. Hydrocodone also affects the center that controls respiratory function, and may produce irregular and periodic breathing. If significant respiratory depression occurs, it may be anticipated by the use of naloxone hydrochloride. Apply other supportive measures when indicated. DRUG ABUSE AND DEPENDENCE: VICODIN/VICODIN ES Tablets are subject to the Federal Controlled Substance Act (Schedule III). Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, VICODIN/VICODIN ES Tablets should be prescribed and administered with caution. OVERDOSAGE: Acetaminophen Signs and Symptoms: In acute acetaminophen overdose, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypotension, coma, and thrombocytopenia may also occur. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion. Hydrocodone Signs and Symptoms: Serious overdose with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and tidal volume), Cheyne-Stokes respiration, (cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur.
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 275 MG TABLETS
Anaprox® DS Anaprox®
(NAPROXEN SODIUM)

SYNTAX
SYNTEX PHARMACEUTICALS INC. A SUBSIDIARY OF SYNTAX INTERNATIONAL
This message could be one of encourage-ment 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 it is to treatment and 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.
HELP PREVENT HEART ATTACK WITH A STROKE.

The back stroke. The crawl. The butterfly. It doesn’t matter which you choose, as long as you do it up to 40 minutes, 3 to 4 times a week. Or try cycling or jogging. Any type of aerobic exercise program can help reduce your risk of heart attack and stroke. The only hard part is diving in. To learn more, contact the American Heart Association, 7272 Greenville Avenue, Box 47, Dallas, TX 75231-4596.

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

American Heart Association

---

Combining Control and Confidence

Control

- Premixed to provide rapid onset and sustained duration

Confidence

- Premixed so patients don’t have to mix for themselves
- Simple, B.I.D. dosage

WARNING: ANY CHANGE IN INSULIN SHOULD BE MADE CAUTIOUSLY AND ONLY UNDER MEDICAL SUPERVISION.

Novolin® is a trademark of Novo Nordisk A/S. © 1992 Novo Nordisk Pharmaceuticals Inc. 208-62 November 1992 Printed in U.S.A.
24-HOUR DELIVERY FOR 24-HOUR SECURITY

DILOXOR XR (diloxor HCl)

BRIEF SUMMARY

CONTRAINDICATIONS
Diloxor hydrochloride is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning pacemaker; (2) patients with second or third degree AV block except in the presence of a functioning ventricular pacemaker; (3) patients with hypotension (less than 90 mm Hg systolic); (4) patients who have demonstrated hypersensitivity to the drug; and (5) patients with acute myocardial infarction and pulmonary congestion as documented by X-ray on admission.

WARNINGS

1. Congestive Heart Failure. Diloxor hydrochloride prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome or second or third degree AV block) of 40 to 10.119, patients, or 5.12% of those 60 mg patients had angina pectoris and/ or had significant ventricular conduction defects (i.e., 2 or 5 seconds after a single 60 mg dose of diloxor.

2. Congestive Heart Failure. Although diloxor has a negative inotropic effect in isolated animal tissue preparations, the hemodynamic effect of diloxor in humans in patients with congestive heart failure has not been adequately studied. The use of diloxor hydrochloride in combination with beta-blockers in patients with impaired ventricular function is restricted.

3. Hypotension. Decrease in blood pressure associated with diloxor hydrochloride therapy may occasion rapidly symptomatic hypotension.

4. Acute Hepatic Injury. Mild elevations of serum transaminases with or without concomitant elevation in alkaline phosphatase and bilirubin have been observed in clinical studies. Such elevations were usually transient and resolved even with continued diloxor therapy. In the instance of significant elevations in alkaline phosphatase, LDH, SGOT, SGPT, and other phenomena consistent with acute hepatic injury have been noted. These reactions tended to occur early after therapy initiation (1 to 6 weeks) and have been reversible upon discontinuation of drug therapy. The relationship to diloxor is uncertain in some cases, but probably in others (see PRECAUTIONS).

PRECAUTIONS

General. Diloxor hydrochloride is extensively metabolized by the liver and is excreted by the kidney and in bile. Drug given in overdosage should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal function. In specific cases of drug-induced toxic symptoms, dose of 125 mg of diloxor and higher in rats was associated with the histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were associated with hepatic changes; however, these changes were reversed with continued dosage.

Drug-Drug Interactions (see ADVERSE REACTIONS). Drug Therapy can be administered simultaneously, but should be avoided simultaneously. Drug-Drug Interactions (see ADVERSE REACTIONS). Drug Therapy can be administered simultaneously, but should be avoided simultaneously.

Pregnancy. Category C. Reproduction studies have been conducted in mice and rats. Administration of doses ranging from 4 to 6 times depending on species the upper limit of the dosage range in clinical trials (400 mg c.i.d. or 8 mg/kg c.i.d. for a 60-kg patient) has resulted in embryo and fetal lethality. These studies have involved animals in which the potential to induce abnormalities of the skeleton, heart, retina, and tongue. Also observed are reductions in early individual pup weights and pup survival, prolonged delivery, and increased incidence of stillbirths. There are no well-controlled studies in pregnant women; therefore, use diloxor hydrochloride in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diloxor is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If the use of diloxor hydrochloride is deemed essential, an alternative method of infant feeding should be instituted.

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

ADVERSE REACTIONS
Serious adverse reactions to diloxor hydrochloride have been rare in studies with other formulations, as well as with Diloxor XR. It should be recognized, however, that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded from these studies.

The most common adverse events (frequency >1% in placebo-controlled clinical hypertension studies with Diloxor XR using daily doses up to 540 mg) are listed in the table below with placebo-treated patients included for comparison.

MOST COMMON ADVERSE EVENTS IN DOUBLE BLIND, PLACEBO CONTROLLED HYPERTENSION TRIALS

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Diloxor XPr</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Event</td>
<td>308 (4%)</td>
<td>287 (4%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>290 (4%)</td>
<td>271 (3%)</td>
</tr>
<tr>
<td>Headache</td>
<td>278 (4%)</td>
<td>215 (3%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>172 (2%)</td>
<td>125 (2%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>113 (2%)</td>
<td>96 (2%)</td>
</tr>
<tr>
<td>Cough</td>
<td>95 (1%)</td>
<td>72 (1%)</td>
</tr>
<tr>
<td>Flu syndrome</td>
<td>70 (1%)</td>
<td>55 (1%)</td>
</tr>
<tr>
<td>Edema, peripheral</td>
<td>70 (1%)</td>
<td>55 (1%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>70 (1%)</td>
<td>55 (1%)</td>
</tr>
<tr>
<td>Abnormalities</td>
<td>50 (1%)</td>
<td>35 (1%)</td>
</tr>
<tr>
<td>Pain, back</td>
<td>50 (1%)</td>
<td>35 (1%)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>20 (1%)</td>
<td>10 (1%)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>20 (1%)</td>
<td>10 (1%)</td>
</tr>
<tr>
<td>Injury, accident</td>
<td>10 (1%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Anorexia, abdominal</td>
<td>10 (1%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>30 (1%)</td>
<td>20 (1%)</td>
</tr>
</tbody>
</table>

*Adverse events occurring in 1% or more of patients receiving Diloxor XR.

The following additional events (COSTART Terms), listed by body system, were reported infrequently in all subjects and hypertensive patients who received Diloxor XR (n=420): Cardiovascular: First-degree AV block, arrhythmia; postural hypotension, tachycardia, palpitations, chest pain, ECG abnormality; nervous system: vertigo, dizziness, syncope; Digestive System: dry mouth, anorexia, tongue disorder, eructation; Skin and Appendages: sweating, urticaria, skin hyperesthesia (heaval); Respiratory System: dyspnea; Respiratory Disorder: Urticaria; Gastrointestinal System: constipation; kidney calculi, impotence, dysmenorrhea, vaginitis, prostate disease; Metabolic and Nutritional Disorders: Gastric, edema, Musculoskeletal System: Arthritis, bursitis, bone pain; Hemic and Lymphatic System: Lymphadenopathy; Body as a Whole: Voiding, urination, urination, urination, urination, urination, urination.

OVERDOSE OR AGGRAVATED RESPONSE
Overdosage experience with oral diloxor hydrochloride has been limited. The administration of iposap to induce vomiting and activated charcoal to reduce drug absorption have been advocated as initial means of intervention. In addition to gastric lavage, the following measures should also be considered.

Breadcrumbs: Administer atropine (0.06 to 0.1 mg). If there is no response to vagal blockade, administer atropine intravenously.

Cardiac Failure: Administer inotropic agents (dobutamine or dobutamine dibromide) and diuretics.

Hypotension: Vasopressors (epinephrine or levodopa/levodopa).

Actual treatment and dosage should depend on the severity of the clinical situation as well as the judgment and experience of the treating physician.

Do not use vasopressors or plasma concentrations after a standard dose of diloxor can vary over time, which significantly limits their value in evaluating cases of overdose.

Charcoal hemoperfusion has been used successfully as an adjunct therapy to hasten drug elimination. Overdoses with as much as 10.9 g of oral diloxor have been successfully treated using appropriate supportive care.

CAUTION: FEDERAL (USA) LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

Please see product circular for full prescribing information.

RHÔNE-POULENC RORER PHARMACEUTICALS INC.

2401 ARCOLA ROAD

COLLEGEVILLE, PA 19426


©1993 Rhone-Poulen Rorer Pharmaceuticals Inc.
Now, for hypertension
Once-a-day
DILACOR XR
(diltiazem HCl)
EXTENDED RELEASE CAPSULES

NEW 120-mg strength for patients who need the lowest starting dose

1 = 24 HOUR SECURITY

DILACOR XR effectively lowers blood pressure for 24 hours in the majority of patients\(^1\)

DILACOR XR offers the classic diltiazem safety profile across the entire dosing range\(^1\)

DILACOR XR now makes diltiazem a more affordable option for hypertension*

Please see adjacent page for brief summary of prescribing information.

Bioethics

The critical questions fall in the gray.

Announcing grants in bioethics from The Greenwall Foundation

With the promises of modern science come moral dilemmas for us as medical professionals, for patients and for society as a whole. We must face questions as new as “who holds the patent to genetically-engineered cells?” ... and as old as “what is life?”

Funding crosses disciplines
The Greenwall Foundation’s Interdisciplinary Program in Bioethics provides modest funding for physicians, lawyers, philosophers, economists, theologians and other professionals to address issues in bioethics. The program supports projects designed to provide guidance for those engaged in decision-making at the bedside as well as those responsible for shaping institutional and public policy.

Whether you are interested in applied research in bioethics, the development of educational programs on ethical concerns, or contributing to the public discussion of medicoethical issues and policy options, The Greenwall Foundation might be able to help.

Make your application now
To apply for limited funding, send a letter outlining:

• your project objectives and how you plan to attain them
• a summary budget, specifying the amount requested from the Foundation
• a statement of the qualifications of the project director, and
• a copy of the sponsoring institution’s annual report with financial data.

Write to:
The Greenwall Foundation
Two Park Avenue (24th Floor)
New York, NY 10016

The next deadline for applications is August 1.
AUTHORSHIP RESPONSIBILITY, FINANCIAL DISCLOSURE, AND ASSIGNMENT OF COPYRIGHT

Each author must read and sign (1) the statement on authorship responsibility; (2) the statement on financial disclosure; and (3) either the statement on copyright transfer or the statement on federal employment. If necessary, photocopy this document to distribute to coauthors for their signatures. Please return all copies to the address below.

1. Authorship Responsibility
I certify that I have participated sufficiently in the conception and design of this work and the analysis of the data (where applicable), as well as the writing of the manuscript, to take public responsibility for it. I believe the manuscript represents valid work. I have reviewed the final version of the manuscript and approve it for publication.

Author(s) Signature(s)

Neither this manuscript nor one with substantially similar content under my (our) authorship has been published or is being considered for publication elsewhere, except as described in an attachment.

Furthermore, I attest that I shall produce the data upon which the manuscript is based for examination by the editors or their assignees should they request it.

Date Signed

2. Financial Disclosure
I certify that I have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript (eg.

Author(s) Signature(s)

employment, consultancies, stock ownership, honoraria), except as disclosed in an attachment.

Any financial project support of this research is identified in an acknowledgment in the manuscript.

Date Signed

3. Copyright
In compliance with the Copyright Revision Act of 1976, effective January 1, 1978, the American Medical Association (AMA), in consideration of taking further action in reviewing and editing your submission, requests that each author sign a copy of this form before manuscript review can proceed. Such signature shall evidence the mutual understanding between the AMA and

Author(s) Signature(s)

the undersigned author(s) thereby transferring, assigning, or otherwise conveying all copyright ownership, including any and all rights incidental thereto, exclusively to the AMA.

In consideration of the action of the AMA in reviewing and editing this submission, the author(s) undersigned hereby transfer(s), or otherwise convey(s) all copyright ownership to the AMA in the event that such work is published by the AMA.

Date Signed

US Federal Employees: If you are an employee of the US federal government, please sign the following statement: I was an employee of the US federal government when this work was

Author(s) Signature(s)

conducted and prepared for publication; therefore, it is not protected by the Copyright Act and there is no copyright, thus ownership cannot be transferred.

Date Signed

Return the original signed form to Marjorie A. Bowman, MD, MPA, Editor, Archives of Family Medicine, Bowman Gray School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1084. Retain one copy for your files. (Photocopies may be made as needed.)
Hurricane Andrew destroyed more than homes.

Andrew blew away the practices of nearly 1000 physicians.

Offices and equipment were flattened, patient and financial records were destroyed, and carefully nurtured careers were shattered ... all in a matter of hours. Now, the mammoth task of rebuilding southern Florida is underway.

Many of your Florida colleagues need help fast—their losses go far beyond what can be covered by insurance or government assistance. At the same time, their patients’ need for skilled care is at a critical high.

The Florida Medical Foundation/Hurricane Relief Fund has been established to help the physicians who were hardest hit in the recent disaster. Your tax-deductible contribution will directly benefit colleagues who are facing the challenge of a lifetime.

The American Medical Association joins the Florida Medical Association in appealing for your help. Send your contribution—or volunteer your services—but don’t hesitate. Act now.

There is much to do, and no time to lose.

Send contributions payable to: Florida Medical Foundation, Hurricane Relief Fund, PO Box 2411, Jacksonville, FL 32203. Or contact the Florida Medical Association, 904 356-1571.
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. 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


© 1992 Syntex Puerto Rico, Inc. NP92161