Today's hypertensives with new concerns...

THE CARDURA GENERATION

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

Choose CARDURA for around-the-clock blood pressure control that doesn't jeopardize blood lipids or blood sugar. Choose CARDURA for around-the-clock blood pressure control that doesn't jeopardize blood lipids or blood sugar. 2-4

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%).

Please see brief summary of prescribing information on next page.

©1993, Pfizer Inc

ONCE-A-DAY CARDURA

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

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

**Summary of Product Characteristics**

**INDICATIONS AND USAGE**

CARDAVR (doxazosin mesylate) is indicated for the treatment of hypertension. CARDAVR may be used alone or in combination with diuretics or beta-blocker and/or angiotensin-converting enzyme (ACE) inhibitors and/or insulin sensitizers. It is not known whether this drug will affect the results of laboratory tests for patients who are taking other medications. CARDAVR may also be used in combination with calcium channel blockers or other antihypertensive agents.

**CONTRAINDICATIONS**

CARDAVR is contraindicated in patients with a known sensitivity to quinazolines, including those with diabetes mellitus, end-stage renal disease, hepatic impairment, severe renal impairment, or congestive heart failure.

**WARNINGS**

Sepsis and "First-Dose" Effect:

Doxazosin, like other alpha-adrenergic blocking agents, may cause marked suppression of the renin-angiotensin-aldosterone axis, resulting in hypotensive episodes, sinus bradycardia, and peripheral edema. Doxazosin may also cause reflex tachycardia that may be associated with a drop in blood pressure. This effect is more common in patients who have been receiving other antihypertensive medications or who have been treated with antihypertensive drugs such as diuretics or beta blockers. In patients with severe cardiac disease, this effect may lead to reflex tachycardia and/or a decrease in cardiac output, which may result in syncope or cardiac arrest. Doxazosin should be used with caution in patients with a history of cardiac disease, and in patients who are taking medications that may cause hypotension, including vasodilators, nonsteroidal anti-inflammatory drugs, and antidepressants. Doxazosin may also cause symptoms of urinary retention, including hesitancy, frequency, urgency, and nocturia. These symptoms have been reported in patients with prostatic hypertrophy. Doxazosin is not recommended for use in patients with severe cardiac disease, including those with severe aortic stenosis, severe mitral stenosis, or severe conduction defects. Doxazosin should be used with caution in patients with severe renal impairment, severe hepatic impairment, or severe pulmonary conditions.

**ADVERSE REACTIONS**

**CARDAVR TOXICITY IN ANIMALS:**

An increased incidence of fatal necropsy or necrotic lesions was observed by Sprague-Dawley rats after 6 months of dietary administration to concentrations calculated to provide 40 mg doxazosin/kg/day. A 100x times the maximum recommended human dose assuming a weight of 60 kg. Monophasic tumors were observed in both rats and mice treated in the same manner with 46 mg doxazosin/kg/day for 18 months. Necrotic lesions were observed at lower doses (4 to 10 mg/kg) in dogs, and occasionally observed on the study in either species. These lesions were not observed after 12 months of oral dosing in dogs and were not observed after 12 months of dietary administration to either species. The morbid study, however, was compromised by the failure to use a maximally tolerated dose of doxazosin.

**CAROTIDODENOMA, Mucocutaneous and Inflammation of Fertility:**

CARDAVR should be stopped at least 24 hours before major surgery (open heart surgery, and open surgery for hypertension). Niemann-Pick disease should be used with caution in patients with severe cardiac disease, including those with severe aortic stenosis, severe mitral stenosis, or severe conduction defects. Doxazosin should be used with caution in patients with severe renal impairment, severe hepatic impairment, or severe pulmonary conditions.

**PRECAUTIONS**

1. **Oral Hypertension:**

While doxazosin is the most severe adverse effect of CARDAVR, other symptoms of lower blood pressure, such as dizziness, light-headedness, or vertigo, can occur, especially at initiation of therapy or at the time of dose increase. These symptoms are more common in patients taking drugs that block the renin-angiotensin system or who are taking diuretics. These symptoms may be related to a decrease in intravascular volume and may be associated with a decrease in blood pressure. These symptoms may be more pronounced in patients who are taking other antihypertensive medications or who have been treated with antihypertensive drugs such as diuretics or beta blockers. Doxazosin may also cause symptoms of urinary retention, including hesitancy, frequency, urgency, and nocturia. These symptoms have been reported in patients with prostatic hypertrophy. Doxazosin is not recommended for use in patients with severe cardiac disease, including those with severe aortic stenosis, severe mitral stenosis, or severe conduction defects. Doxazosin should be used with caution in patients with severe renal impairment, severe hepatic impairment, or severe pulmonary conditions.

2. **Improved liver function:**

Patients should be monitored for the development of severe liver disease or jaundice, hepatic encephalopathy, or other serious liver disease. Patients with hepatic disease or jaundice should be treated with caution.

3. **Leukopenia/Neutropenia:**

A positive correlation was observed between patients receiving CARDAVR in controlled clinical trials that showed the mean WBC (IR) and neutrophil counts (IR+4) were decreased by 2.4% and 0.3% respectively, compared to placebo. Neutropenia, anemia, and leucopenia were observed in patients taking doxazosin, and are reversible after discontinuation of the drug. As a result, patients should be monitored for signs of bone marrow depression during treatment with CARDAVR.

4. **Anaphylactoid reactions:**

A positive correlation was observed between patients receiving CARDAVR in controlled clinical trials that showed the mean WBC (IR) and neutrophil counts (IR+4) were decreased by 2.4% and 0.3% respectively, compared to placebo. Neutropenia, anemia, and leucopenia were observed in patients taking doxazosin, and are reversible after discontinuation of the drug. As a result, patients should be monitored for signs of bone marrow depression during treatment with CARDAVR.

5. **Peripheral edema:**

Peripheral edema was observed in patients taking CARDAVR, and is reversible after discontinuation of the drug. As a result, patients should be monitored for signs of bone marrow depression during treatment with CARDAVR.

6. **SKIN ADAPTEMENTS:**

A positive correlation was observed between patients receiving CARDAVR in controlled clinical trials that showed the mean WBC (IR) and neutrophil counts (IR+4) were decreased by 2.4% and 0.3% respectively, compared to placebo. Neutropenia, anemia, and leucopenia were observed in patients taking doxazosin, and are reversible after discontinuation of the drug. As a result, patients should be monitored for signs of bone marrow depression during treatment with CARDAVR.

**DIAGNOSIS**

CARDAVR should be used with caution in patients with severe cardiac disease, including those with severe aortic stenosis, severe mitral stenosis, or severe conduction defects. Doxazosin should be used with caution in patients with severe renal impairment, severe hepatic impairment, or severe pulmonary conditions.

6. **SKIN ADAPTEMENTS:**

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**TABLE 1**

**ADVERSE REACTIONS DURING PLACED CONTROLLED STUDIES**

**DOXAZOSIN**

Placebo

**INDICATIONS**

CARDAVR (doxazosin mesylate) Tablets

**COMMENTS**

CARDAVR is not recommended for use in patients with severe cardiac disease, including those with severe aortic stenosis, severe mitral stenosis, or severe conduction defects. Doxazosin should be used with caution in patients with severe renal impairment, severe hepatic impairment, or severe pulmonary conditions.

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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.

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.

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.

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.
VERELAN
AS EFFECTIVE AS PROCARDIA XL®
IN REDUCING BP AT THE 24TH HOUR

Reduction in mean DBP measured 24±2 hours after dosing

Results of a 12-week, randomized, double-blind, parallel, comparative study of patients with mild-to-moderate hypertension in 10 study sites nationwide. Patients not controlled on VERELAN 240 mg/day were titrated to 360 mg/day and, if needed, 480 mg/day; patients not controlled on Procardia XL 30 mg/day were titrated to 60 mg/day and, if needed, 90 mg/day. There was no significant difference between groups in the number of titrations to goal DBP (<90 mm Hg).

*Procardia XL is a registered trademark of Pfizer Inc.

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 on adjacent page.

ONCE-A-DAY
VERELAN
Verapamil HCl
120 mg
180 mg
240 mg
PELLET-FILLED CAPSULES
Living in Medicine

'My Daughter Thinks She's Pregnant'
Anne D. Walling, MD

Corporal Punishment
Patrick F. Mongan, MD

In Reply
Kenelm F. McCormick, MD

Depression or Oppression?
Louise Acheson, MD

Early Detection of Domestic Abuse
Bill C. DeMoss, MD

Commentary

The Discovery of Ether Anesthesia:
Jumping on the 19th-Century Bandwagon
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A Structured Literature Review of Treatment for Localized Prostate Cancer
John H. Wasson, MD; Cynthia C. Cushman, MD; Reginald C. Brushewitz, MD; Benjamin Littenberg, MD; Albert G. Mulley, Jr, MD, MPP; John E. Wennberg, MD, MPH; and the Prostate Disease Patient Outcome Research Team

Cefaclor vs Amoxicillin in the Treatment of Acute, Recurrent, and Chronic Sinusitis
Werner Huck, M(ASCP); Barbara D. Reed, MD, MSPH; Richard W. Nielsen, MD; Robert T. Ferguson, MD; Dean W. Gray, MD; Glen K. Lund, MD; Dean H. ZoBell, MD; Mary Beth Moster

Original Contributions

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While every precaution is taken to ensure accuracy, we cannot
guarantee against the possibility of an occasional change
or omission in the preparation of this index.
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 125 mg/day may be warranted in some patients. In elderly patients or those with small stature, dosages above 240 mg/day should be administered in divided doses. Calan SR should be administered with food. Constipation, which is easily managed in most patients, is the most common reported side effect of Calan SR.

BRIEF SUMMARY

Contraindications: Severe LV dysfunction (see Warnings), hypertension (systolic pressure <30 mm Hg) or cardiogenic shock, sick sinus syndrome if pacemaker is present, 2nd- or 3rd-degree AV block (if no pacemaker is present) and ateriovenous fistula with an accessory bypass tract (eg, PKW or LGL syndromes), hypersensitivity to verapamil.

Warnings: Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction <30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control of hypertensive patients with 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. Severe cases have been demonstrated by peripheradamiolism. Periodic monitoring of liver function is in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/infrequent and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased OR:AV conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving T:verapamil (oral or digital). Because of this risk, oral verapamil may be contraindicated in such patients. AV block may occur (2nd- or 3rd-degree, 1.0% of cases). 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 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 (as severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdose. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to increase verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction, and/or cardiac contractility. The same concern has been expressed with other agents that similarly increase cardiac contractility and reduce heart rate and contractility. Decreased myocardial and propofol clearance may occur in patients with hepatic cirrhosis, verapamil may reduce total body clearance and renal clearance of digitoxin. The digitoxin dose should be reduced when verapamil is given, and the patient closely monitored. Verapamil is usually an additive effect in patients receiving blood-pressure-lowering agents.

Disopyramide should not be given within 48 hours before, or 24 hours after verapamil administration. Concomitant use of tiofanil and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypotrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in an increased tendency to lithium (hepatic) and an increase in serum lithium levels, however, it may also result in a lowering of serum lithium levels. Patients receiving both drugs must be monitored carefully. Verapamil may increase cardiac conduction concentrations during combined use. Rhabdomyolysis may result in increased serum levels of creatine kinase. Verapamil may induce the clearance and increase the clinical levels of theophylline. Combined use of heparin and verapamil may result in increased bleeding time and excessive anticoagulant depression. Verapamil may potentiate the activity of neuromuscular blocking agents (atracurium and vecuronium). 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 carcinogenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk, therefore, nursing should be discontinued during verapamil use.

Adverse Reactions: Constipation (7.3%), dizziness (1.3%), nausea (2.7%), hypertension (2.5%), headache (2.3%), edema (1.9%), cough (1.7%), dyspnea (1.9%), bradycardia (0.4% to 5.0%), AV block, total:1.3% to 2.3%, 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes, reversible non-obstructive paralytic ileus. The following reactions, reported in 10% or less of patients, occurred under conditions when a causal relationship is uncertain: anuria, paresthesia, postural hypotension, chest pain, claudication, myoclonus, palpitations, paresthesias, paresthesia, syncope, diarrhea, dry mouth, gastralgia, digestive disorders, pyrexia, eosinophilia, pruritus, bradycardia, edema, urticaria, angioedema, angina, muscle cramps, headache, myalgia, seizures, insomnia, confusion, dysarthria, urinary tract disorder, tumor, vision, hypothyroidism, increased creatinine, hypotension, impotence.
Now lactose-free doesn’t

The “best of both worlds” in an everyday formula
have to mean milk-free!

More like breast milk than other lactose-free formulas

<table>
<thead>
<tr>
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<th>PROTEIN</th>
<th>FAT</th>
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<tr>
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<td>LACTOSE</td>
<td>HUMAN MILK PROTEIN</td>
<td>HUMAN MILK FAT</td>
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<td>Milk-Based Formula</td>
<td>LACTOSE</td>
<td>MILK PROTEIN</td>
<td>VEGETABLE OIL BLEND*</td>
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<td>Lactofree™</td>
<td>LACTOSE FREE</td>
<td>MILK PROTEIN</td>
<td>VEGETABLE OIL BLEND</td>
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<tr>
<td>Soy-Based Formula</td>
<td>LACTOSE FREE</td>
<td>SOY PROTEIN</td>
<td>VEGETABLE OIL BLEND*</td>
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The benefits of milk protein without the problems of lactose

- Keeps milk protein—the preferred protein source—in the infant's diet
- Avoids or resolves common feeding problems associated with lactose:
  - fussiness/crying  - gas  - diarrhea
- Easy to digest
- No other formula has a fat blend closer to breast milk

Recommend...

Lactofree

Lactose-Free Formula for Baby's First Year and Beyond

The first milk-based formula with the lactose-free difference

* SMA® and Nusoy® (registered trademarks of Wyeth-Ayerst Laboratories, Philadelphia, PA) contain some animal fats.
† Data on file, Mead Johnson & Company
©1993, Mead Johnson & Company, Evansville, Indiana 47721, U.S.A.
L-K370-4-93
‡ We know of no studies showing clinical benefits from fatty acid profiles closer to breast milk, but Mead Johnson believes such profiles are prudent and appropriate.
§ Based on milk protein isolate
A Clinical Demonstration of
MIGRAINE RELIEF
YOU CAN SEE IN MINUTES

11:00 a.m.

11:13 a.m.

11:24 a.m.
Actual clinical course of a patient following administration of one 6-mg subcutaneous injection of IMITREX for migraine (time-lapse footage).
MIGRAINE RELIEF THAT CAN CHANGE PATIENTS' LIVES

IMITREX is the first highly specific 5-HT, receptor agonist—offering a profile of relief unlike any other migraine therapy.

Relief that begins within 10 minutes.\textsuperscript{1,2}

Relief any time IMITREX is taken during the attack.\textsuperscript{1,3,4}

Relief of the total symptom complex: pain, nausea, vomiting, and light and sound sensitivity.\textsuperscript{1,4}

Relief of the disability caused by migraine.\textsuperscript{1,4}

Relief without sedation.

Relief in a simple, convenient dose: one 6-mg subcutaneous injection.*

Relief within reach for patients: The IMITREX™ SELFdose System—a push-button autoinjector with single-dose, prefilled syringes.

Relief of migraine attacks with or without aura. (IMITREX should not be administered to patients with basilar or hemiplegic migraine.)

*Maximum daily dose is two 6-mg subcutaneous injections (minimum 1-hour interval between doses). No clear benefit is associated with the administration of a second 6-mg dose in patients who have failed to respond to a first injection.
RELIEF OF THE TOTAL SYMPTOM COMPLEX FAST... ANY TIME

"I've got things to do. I want to function again.... IMITREX gave me a very clean, healthy, normal feeling. I felt restored."

Betty H.
46-year-old migraine sufferer
RELIEF WITHOUT COMPROMISE

IMITREX is highly selective.
IMITREX is nonsedating.
There is no evidence of interactions between IMITREX and prophylactic migraine medications (verapamil, amitriptyline, and propranolol).

Cardiovascular considerations
IMITREX is contraindicated in patients with ischemic heart disease, symptoms or signs consistent with ischemic heart disease, or Prinzmetal's angina because of the potential to cause coronary vasospasm. IMITREX is contraindicated in patients with uncontrolled hypertension because it can give rise to increases in blood pressure (usually small).

Although serious coronary events are extremely rare, consideration should be given to administering the first dose of IMITREX in-office to patients in whom unrecognized coronary disease is comparatively likely.

Pregnancy category C
There are no adequate and well-controlled studies in pregnant women; IMITREX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. (Please see Precautions.)

Worldwide clinical experience
IMITREX has been utilized by over 6,000 patients, treating more than 10,000 attacks in well-controlled clinical trials.

Reported adverse events are generally mild and transient.

<table>
<thead>
<tr>
<th></th>
<th>IMITREX (6 mg) (n=547)</th>
<th>Placebo (n=570)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical sensations</td>
<td>42.0%</td>
<td>9.2%</td>
</tr>
<tr>
<td>Tingling</td>
<td>13.5%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Warm/hot sensation</td>
<td>10.8%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>7.5%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Feeling of heaviness</td>
<td>7.3%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Pressure sensation</td>
<td>7.1%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Feeling of tightness</td>
<td>-5.1%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Flushing</td>
<td>6.6%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Injection-site reaction</td>
<td>58.7%</td>
<td>23.8%</td>
</tr>
<tr>
<td>Dizziness/Vertigo</td>
<td>11.9%</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

Most adverse events were mild and resolved spontaneously within 10 to 30 minutes.
Withdrawals due to adverse events are comparable to those seen with placebo (≤3.5% in controlled clinical trials).

For a complete listing of side effects, please consult Brief Summary of Prescribing Information on the last page of this advertisement.
MIGRAINE RELIEF THAT CAN CHANGE PATIENTS' LIVES

RELIEF WITHIN REACH FOR PATIENTS

The IMITREX® SELFdose System: a push-button autoinjector with single-dose, prefilled syringes.

Allows patients to self-administer IMITREX whenever and wherever migraine strikes.

High patient acceptance. — 92% of patients who self-administered IMITREX would be willing to take it again.

Efficacy equivalent to physician-administered IMITREX.

For use only by patients for whom a 6-mg dose has been prescribed.

IMITREX offers simple, convenient dosing.

The recommended dose is one 6-mg subcutaneous injection.

If migraine symptoms return, a second 6-mg dose may be administered.

The maximum dose within 24 hours is two 6-mg subcutaneous injections (minimum 1-hour interval between doses).

No clear benefit is associated with the administration of a second 6-mg dose in patients who have failed to respond to a first injection.

Although the recommended dose is 6 mg, if side effects are dose limiting, then lower doses may be used.

IMITREX should not be used within 24 hours of administration of ergotamine-containing preparations.

IMITREX™ (sumatriptan succinate) Injection

For Subcutaneous Use Only.

A summary is a summary only, before prescribing, see complete prescribing information in IMITREX™ injection product labeling).

INDICATIONS AND USAGE: IMITREX™ injection is indicated for the acute treatment of migraine headaches, with or without aura, in adult patients. IMITREX injection is not indicated for the preventive treatment of migraine. IMITREX injection is not indicated for the prophylaxis of chronic daily headache. IMITREX injection should not be given to patients with a history of coronary artery disease (CAD), peripheral vascular disease (PVD), or aortic stenosis.

Contraindications: IMITREX injection should not be given to patients with a history of CAD, PVD, or aortic stenosis.

Caution: When given intravenously to patients with CAD, IMITREX injection may cause transient elevation of blood pressure, thus increasing the risk of myocardial ischemia, who are known to be particularly susceptible to the effects of ergot alkaloids.

Pregnancy: There are no adequate and well-controlled studies in pregnant women. IMITREX injection should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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

Use in the Elderly: In clinical studies, safety and effectiveness of IMITREX injection in individuals over age 65 have not been systematically evaluated. However, the pharmacokinetic disposition of IMITREX injection in the elderly is similar to that seen in younger adults. No dosage adjustment is recommended.

Nursing Mothers: IMITREX is excreted in breast milk in minimal amounts. No data exist in humans. Therefore, caution should be exercised when considering IMITREX injection in nursing women.

Pediatric Use: Use of IMITREX injection in children has not been established. Use in the elderly: Safety and effectiveness of IMITREX injection in elderly patients have not been systematically evaluated, but no dosage adjustment is recommended.

Controlled Clinical Trials: In the controlled clinical trials, the most common side effects were chest pain, flushing, tingling sensations, abdominal pain, and diarrhea. These side effects were usually mild to moderate in intensity. In controlled clinical trials of IMITREX injection involving 547 patients, the incidence of side effects was as follows: A total of 41 patients (7.5%) reported chest pain, flushing, tingling sensations, abdominal pain, and diarrhea as serious side effects. A total of 99 patients (18.2%) reported chest pain, flushing, tingling sensations, abdominal pain, and diarrhea as moderate side effects. A total of 319 patients (59.2%) reported chest pain, flushing, tingling sensations, abdominal pain, and diarrhea as mild side effects. A total of 110 patients (20.2%) reported chest pain, flushing, tingling sensations, abdominal pain, and diarrhea as asymptomatic findings.
Interventions: The DT-aP vaccines contained 23.4 µg each of pertussis toxin and filamentous hemagglutinin per 0.5 mL and the same concentrations of diphtheria and tetanus toxoids as WC-DTP. Serum samples were obtained on the day of immunization and 4 to 6 weeks later. Adverse reactions at 6, 24, 48, and 72 hours were recorded by parents who were contacted by telephone at 24 and 72 hours and 14 days after immunization.

Measurements/Main Results: An indirect enzyme-linked immunosorbent assay method was used to determine IgG antibody response to pertussis toxin and filamentous hemagglutinin and IgG, IgA, and IgM to tetanus toxoids; a Chinese hamster ovary cell assay was used to measure functional antibodies to pertussis toxin; serum neutralization on VERO cells assayed diphtheria antitoxin. Recipients of the DT-aP vaccine had fewer local reactions in the first 6 to 48 hours and fewer systemic reactions at 24 hours than did recipients of the WC-DTP vaccine. Acetaminophen was administered to 31% of DT-aP recipients compared with 63% of WC-DTP recipients. Infants given DT-aP had higher geometric mean antibody titer levels against pertussis antigens after vaccination.

Conclusions: The BIKEN DT-aP vaccine used in this study is less reactogenic and more immunogenic for selected pertussis antigens than the WC-DTP vaccine in children aged 15 to 20 months.

(1993;147:290-294) John F. Marcinak et al, MD, Department of Pediatrics (M/C 856), The University of Illinois at Chicago, 840 S Wood St, Chicago, IL 60612.

 ARCHIVES OF SURGERY

Can Patients With Minor Head Injuries Be Safely Discharged Home?

To identify all patients with serious intracranial injury, current treatment strategies include admission and/or computed tomographic evaluation of all patients with head injuries. However, the majority of patients with head injuries who are awake do not require subsequent intervention. A review of 407 consecutive patients with head injuries treated at an adult regional trauma center identified 310 patients with Glasgow Coma Scores of 15 in the emergency department, all of whom were admitted. Five patients with Glasgow Coma Scores of 15 required intervention for intracranial abnormality. All five patients had skull fractures and/or neurologic deficits. Based on this and other studies, criteria for discharge from the emergency department are a Glasgow Coma Score of 15, no deficit except amnesia, no signs of intoxication, and no evidence of basilar fracture on clinical examination or linear fracture on screening skull roentgenography. Safe discharge without universal computed tomographic evaluation or admission is possible and cost-efficient.
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 lipids. 1,4 And unlike Dyazide® or Maxzide, 3 there may be no increased risk of hyperkalemia when LOZOL is used in combination with ACE inhibitors.

Calcium excretion is decreased by thiazides 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 thyrotoxicosis. Concomitant use of anticoagulant drugs increases the risk of bleeding. Indapamide is metabolized in the liver and excreted by the kidneys. In patients with impaired renal function, the dose of indapamide should be reduced. Calcium excretion is decreased by thiazides 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 thyrotoxicosis. Concomitant use of anticoagulant drugs increases the risk of bleeding. Indapamide is metabolized in the liver and excreted by the kidneys. In patients with impaired renal function, the dose of indapamide should be reduced. Calcium excretion is decreased by thiazides 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 thyrotoxicosis. Concomitant use of anticoagulant drugs increases the risk of bleeding. Indapamide is metabolized in the liver and excreted by the kidneys. In patients with impaired renal function, the dose of indapamide should be reduced. Calcium excretion is decreased by thiazides 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 thyrotoxicosis. Concomitant use of anticoagulant drugs increases the risk of bleeding. Indapamide is metabolized in the liver and excreted by the kidneys. In patients with impaired renal function, the dose of indapamide should be reduced. Calcium excretion is decreased by thiazides 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 thyrotoxicosis. Concomitant use of anticoagulant drugs increases the risk of bleeding. Indapamide is metabolized in the liver and excreted by the kidneys. In patients with impaired renal function, the dose of indapamide should be reduced.
For pain/inflammation

Rx Anaprox® DS Anaprox®

550 MG TABLETS 275 MG TABLETS

(NAPROXEN SODIUM)

As with other NSAIDs, the most frequent complaints are gastrointestinal. See Warnings, Precautions, and Adverse Reactions sections of prescribing information. Please see adjacent page for brief summary of prescribing information.

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"Ismo® (isosorbide mononitrate) 20 mg tablets"

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULAR.)

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

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

Several well-controlled studies have demonstrated that active nitrates were indistinguishable from placebo after 24 hours (or less) of continuous therapy due to the development of tolerance. Only after nitrates are absent from the body for several hours is their antanginal efficacy restored.

The drug-free interval sufficient to avoid tolerance to isosorbide mononitrate is not completely defined. The only regimen shown to avoid development of tolerance with isosorbide mononitrate involves two daily doses of isosorbide mononitrate that are separated by 12 hours apart, one the second dose of the next day. Taking account of the relatively long half-life of isosorbide mononitrate this result is consistent with those obtained for other organic nitrates.

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

Centralized Allergic Reactions are extremely rare, but do occur. Ismo is contraindicated in patients allergic to it.

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

Precautions GENERAL Severe hypotension, particularly with upright posture, may occur with even small doses. Therefore, use with caution in patients who may be volume depleted or who are already hypotensive. Paradoxical bradycardia and increased angina pectoris may accompany Ismo-induced hypotension.

Nitrates may aggravate angina caused by hypertrophic cardiomyopathy.

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

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

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

DRUG INTERACTIONS Vasodilating effects of Ismo may be additive with those of other vasodilators, especially alcohol.

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

CARCINOGENESIS, MUTAGENESIS, AND IMPAIRMENT OF FERTILITY No carcinogenic effects were observed in mice or rats exposed to oral Ismo, nor were adverse effects on fertility detected.

No mutagenic activity was seen in in vitro or in vivo assays.

PREGNANCY CATEGORY C Ismo has been shown to have embryotoxic effects in rats and rabbits at doses of at least 70 times the maximum human dose. There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if potential benefit justifies potential fetal risk.

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

PEdiAtRIC USE Safety and effectiveness have not been established.

Adverse Reactions Frequency of Adverse Reactions (Discontinuations) Occurring in >1% of Subjects

<table>
<thead>
<tr>
<th>6 Controlled U.S. Studies</th>
<th>92 Clinical Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>Placebo</td>
</tr>
<tr>
<td>Patientes</td>
<td>294</td>
</tr>
<tr>
<td>Headache</td>
<td>9%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1%</td>
</tr>
<tr>
<td>Nausea, Vomiting</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

*Statistically discontinued for multiple reasons

Fewer than 1% of patients reported each of the following (in many cases a causal relationship is uncertain):

Cardiovascular: angina pectoris, arrhythmias, atrial fibrillation, hypotension, palpitations, postural hypotension, presyncope, retrosternal discomfort, syncope, tachycardia, ventricular extrasystoles, vasodilation, chest pain.

Respiratory: nasal or other persistent rhinorrhea, cough, epistaxis.

Gastrointestinal: abdominal pain, diarrhea, dyspepsia, flatulence, nausea, vomiting.

Nervous System: dyscoordination, impotence, malaise, nausea, restlessness, somnolence, sweating, tachycardia.

Psychiatric: anxiety, confusion, depression, dysphoria, euphoria, headache, hyperesthesia, increased agitation, insomnia, nervousness, psychoses, quincke edema, syncope, tremor, twitching.

Skin: pruritus, rash, urticaria.

Other: acute renal failure, fever, headache, ring-around-the-eyes, upper respiratory tract infection.

Rarely, ordinary doses of organic nitrates have caused methemoglobinemia in normal-seeming patients (see Overdosage).

Overdosage The ill effects of overdosage are generally related to the ability of Ismo to induce vasodilation, venous pooling, reduced cardiac output and hypotension. Symptoms may include increased intracranial pressure, visual hallucinations or all of persistent throbbing headache, confusion, and moderate decrease in level of consciousness. Manifestations: visual disturbances; nausea and vomiting (possibly with copious and even bloody diarrhea; syncope (especially with upright posture); air hunger and dyspnea, later followed by reduced ventilatory effort; diaphoresis, with the skin either flushed or cold and clammy; heart block and bradycardia; paraesthesia, coma; seizures and death.

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

There is neither a specific antidote to Ismo overdose, nor data to suggest a means for accelerating its elimination from the body: diuresis is ineffective. Hypotension associated with Ismo overdose results from venodilation and arterial hypotension; therefore, direct therapy toward an increase in central filling volume. Use of arterial vasocostrictors (eg, epinephrine) is likely to do more harm than good. In patients with refractory or CHF treatment of Ismo overdose may be difficult and require invasive ventilation. Methemoglobinemia has occurred in patients receiving other organic nitrates, and probably could occur as a side effect of Ismo. There are case reports of significant methemoglobinemia in association with moderate overdoses of organic nitrates. None of the affected patients had been thought to be unsuitable of therapy. Suspect the diagnosis in patients who exhibit signs of impaired oxygen delivery despite adequate cardiac output and normal arterial pO2. Classically, methemoglobinemia, or ischemia is characterized by a dull, brownish, or slate-gray discoloration in exposed to air. The treatment of choice for methemoglobinemia is methylene blue, 1-2 mg/kg intravenously.

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

Well-controlled studies have shown that tolerance to Ismo tablets is avoided when using the twice daily regimen in which the two doses are given 7 hours apart. This regimen has been shown to provide antanginal efficacy beginning 1 hour after the first dose and lasting at least 5 hours after the second dose. The duration (if any) of antanginal activity beyond 12 hours has not been studied. Large controlled studies with other nitrates suggest that no dosing regimen should be expected to provide more than 12 hours of continuous antanginal efficacy per day.

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

This Brief Summary is based upon the current Ismo direction circular. C41271-1, Issued January 10, 1992.

AHROBINS

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**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.
1. Fungicidal action

- Naftin® is fungicidal, not just fungistatic, to dermatophytes at low concentrations.*
- 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 hydro for the everyday treatment of tinea pedis, tinea crur...
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%

(chloride) 1% Cream and Gel
s and tinea corporis.

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Urination was observed in clinical trials with Naftin® Cream.
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 montage of infected tissue in a solution of potassium hydroxide or by culture on an appropriate medium. Information for patients: The patient should be told to: 1. Avoid the use of occlusive dressing or wrappings 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. Reproduction studies have been performed in rats and rabbits (via oral administration) at doses of 150 times or more the topical human dose and have revealed no evidence of impaired fertility or harm to the fetus due to naftin. 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/stinging (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/stinging (5%), itching (1%), erythema (0.5%), rash (0.5%), skin tenderness (0.5%).

REFERENCES

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AMA / HIV
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A state-of-the-art conference on clinical care of early stage HIV patients. The role of primary care providers in preventing the further spread of HIV by the infected patients will also be addressed.

This conference is intended for physicians and others concerned with the primary care of patients with asymptomatic and mildly symptomatic HIV infection.

For further information contact:
John Henning, PhD
Department of HIV
American Medical Association
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Chicago, IL 60610
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Telephone: 312 464-5460
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As evidenced by well-controlled, long-term studies at more than 40
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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.

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ISOPTIN SR
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Unsurpassed dosage flexibility

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Brief Summary of Prescribing Information

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

WARNINGS: Heart Failure: ISOPTIN should be avoided in patients with severe left ventricular dysfunction 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 and/or chronic atrial flutter or atrial fibrillation and a1 accessory bypass pathway may have developing

ADVERSE REACTIONS: Constipation: 3% to 3.3%. Diarrhea: 2% to 2.6%. Dyspepsia: 2%. Pruritus: 2%. Rash: 2%. Upper respiratory tract infection: 1%. Cough: 1%. Hemorrhage: 1%. Arthralgia: 1%. Gastrointestinal symptoms: 1%. Headache: 1%. Thrombocytopenia: 1%. Anemia: 1%. Eosinophilia: 1%. Myocardial infarction: 1%. Nausea: 1%. Skin rash: 1%. Dyspepsia: 1%. Headache: 1%. Pruritus: 1%. Rash: 1%. Other: 1%

Drug Interactions: Beta Blockers: Concurrent use of ISOPTIN and oral beta-adrenergic blocking agents may result in additive negative effects on heart rate, atrioventricular conduction, and/or cardiac contractility. Excessive bradycardia and AV block, has been reported. The combination should be used only with caution and close monitoring. Digoxin: Clinical use of verapamil in digitized patients has shown the combination to be well tolerated. However, chronic verapamil treatment increases serum digoxin levels by 50% to 75% during the first week of therapy and this can result in digitalis toxicity. Upon discontinuation of ISOPTIN (verapamil HCl), the patient should be reassessed to avoid underdigitalization. Antiarrhythmic Agents: Verapamil administered concurrently with oral antiarrhythmic agents (e.g. quinidine, amiodarone, disopyramide, propranolol) may result in additive effects on conduction and elimination. Arrhythmia Patients: Patients receiving these combinations should be monitored closely. Antiarrhythmic Agents: Disopyramide should not be administered with 48 hours before or 24 hours after verapamil administration. Metoclopramide: Concomitant use of metoclopramide and verapamil may result in additive negative inotropic effect and prolongation of atrioventricular conduction. Quinidine: In patients with hypertrophic cardiomyopathy (HCM), concurrent use of verapamil and quinidine may result in significant hypotension. Other Nitrates: The pharmacologic profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions. Emetine/Verapamil: Variability results on

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., intravenously administered isoproterenol HCl, intravenous bicarbonate, atropine (all in the usual doses), or calcium gluconate (10% solution). If further support is necessary, isotonic agents (dextrose and other electrolytes) may be administered. Actual treatment and dosage should depend on the severity and the clinical situation and the judgment and experience of the treating physician.

OVERDOSAGE: Treatment of overdose should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium salts may increase calcium on 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 cardiac pacing, respectively. Asystole should be handled by the usual measures including cardia

DOSAGE AND ADMINISTRATION


each morning

75 mg, 200 mg each morning
Encouragement

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

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Effective lipid management—improves key lipids

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

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Mean percentage change from baseline after 8 weeks of treatment with 10 to 40 mg of pravastatin:

- LDL-C: -22 to -34%
- Total C: -16 to -25%
- Triglycerides: -11 to -24%
- HDL-C: +2 to +12%
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*Each arrow represents a range of means derived from a single placebo-controlled study that included 55 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%)
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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

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pravastatin sodium 20 mg tablets

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Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the final page of this advertisement.
Intravenous infusions of palivizumab were used in neonates with a dose of 12.5 mg/kg/day, which produced a plasma drug level of about 20 times higher than the mean drug level in humans taking the highest dose (as measured by total antibody titer). This drug also produced ventilator-free days that were significantly prolonged, compared to patients treated with placebo. The difference in mean ventilator-free days between the groups with and without palivizumab was 10 days for patients treated with palivizumab. In patients treated with palivizumab, the dose was increased to 25 mg/kg/day, which produced a mean plasma drug level of about 30 times higher than the mean drug level in humans taking the highest dose. Palivizumab has been shown to be effective in reducing the risk of RSV lower respiratory tract infection among high-risk neonatal infants in studies reviewed by the Cochrane Library. The drug was also shown to be safe and well tolerated in these studies. Palivizumab has been approved by the US Food and Drug Administration (FDA) for use in this population.

However, the benefits of palivizumab treatment in preterm infants have not been consistently observed in all studies. Differences in study design, patient populations, and methodological issues may contribute to these variations. Further research is needed to better understand the optimal use of palivizumab in the prevention of severe RSV disease in high-risk neonatal infants.

Additionally, palivizumab treatment should be individualized based on the risk of severe RSV disease in each patient. The decision to continue or discontinue palivizumab therapy should be made in consultation with a pediatrician or infectious disease specialist, taking into account the patient's clinical status and the potential risks and benefits of treatment.

In conclusion, palivizumab is an effective and well-tolerated prophylactic option for reducing the risk of severe RSV disease in high-risk neonatal infants. However, the use of palivizumab should be individualized, and the decision to continue or discontinue therapy should be made based on a careful assessment of the patient's clinical status and the potential risks and benefits of treatment.
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Reduces the frequency of angina attacks—through 24 hours

**Total angina attacks**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=39)</td>
<td>6.33±1.49</td>
<td>4.43±1.09</td>
</tr>
<tr>
<td>Cardizem CD 100 mg qd (n=37)</td>
<td>3.78±1.06</td>
<td>2.36±0.73</td>
</tr>
<tr>
<td>Cardizem CD 300 mg qd (n=40)</td>
<td>4.51±0.99</td>
<td>1.33±0.41</td>
</tr>
</tbody>
</table>

**On Exertion**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=39)</td>
<td>4.43±1.09</td>
<td>3.40±0.53</td>
</tr>
<tr>
<td>Cardizem CD 100 mg qd (n=37)</td>
<td>3.78±1.06</td>
<td>2.48±0.59</td>
</tr>
<tr>
<td>Cardizem CD 300 mg qd (n=40)</td>
<td>4.51±0.99</td>
<td>1.82±0.38</td>
</tr>
</tbody>
</table>

† At rest and on exertion.

Consistent antihypertensive effect seen throughout 24 hours

- **Ambulatory BP subset**: 4 of 9 sites performed ambulatory BP monitoring. The 47 patients enrolled at these sites were clinically and demographically representative of the total study population. Mean supine cuff DBP at baseline 99.3±0.6 placebo, 99.4±0.7 Cardizem CD.

- **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

*Proven efficacy through 24-hour ambulatory blood pressure recording, peak/trough blood pressure evaluation, and Bruce treadmill protocol.

CCDAH-998/A7534
# 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 3800 patients, the most common events (ie, 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%).

# 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 is available as 60-, 90-, and 120-mg capsules)


Please see brief summary of prescribing information on adjacent page.

**ONCE-A-DAY**

**CARDIZEM® CD**

(diltiazem HCl)
**Once-a-Day Cardizem**

**(diltiazem HCl)** 190-, 180-, 240-, 300-mg Capsules

**24-Hour Control of Both Angina and Hypertension**

**Nursing Mothers**: Diltiazem is excreted in human milk. The report suggests that concentrations in breast milk may approximate serum levels. If Cardizem is deemed essential, an alternative method of infant feeding should be considered.

**Pregnancy**: Safety and effectiveness in children have not been established.

**ADVERSE REACTIONS**

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormality have usually been excluded from these studies.

**In clinical studies**: The incidence of adverse reactions reported during CARIDZEM therapy was not greater than that reported during placebo therapy.

The adverse events described below represent events obtained in clinical studies of hypertensive patients receiving either CARIDZEM tablets or CARIDZEM SR Capsules as well as experiences observed in studies of angina and during monitoring. The most common events in hypertension studies are shown in a table with rates in specific patients shown for comparison. Less common events are listed by body system inclusive of adverse reactions seen in angina studies that were not observed in 1161 hypertension studies. In all hypertensive patients taking CARDIZEM or CARDIZEM SR Capsules studied (over 900), the most common adverse events were edema (8%), headache (6%), dizziness (5%), anorexia (4%), sinus bradycardia (3%), flushing (1%), and first-degree AV block (0.5%). Only edema and perhaps bradycardia and dizziness were dose related.

**Double Blind Placebo-Controlled Hypertension Trials**

| Treatment                      | N Trials | Placebo | Placebo Mean BP *()
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual</td>
<td>1180</td>
<td>1139</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>1180</td>
<td>1139</td>
<td></td>
</tr>
<tr>
<td>200 mg diltiazem</td>
<td>1180</td>
<td>1139</td>
<td>120 ± 11</td>
</tr>
<tr>
<td>100 mg diltiazem</td>
<td>1180</td>
<td>1139</td>
<td>124 ± 12</td>
</tr>
<tr>
<td>50 mg diltiazem</td>
<td>1180</td>
<td>1139</td>
<td>129 ± 14</td>
</tr>
</tbody>
</table>

**In clinical trials of CARDIZEM Capsules, Cardiochem, and Cardizem SR Capsules studied over 3200 patients, the most common events (i.e., greater than 1%) were edema (4%), headache (4%), dizziness (3%), anorexia (2%), orthostatic (2%), first-degree AV block (2.4%), bradycardia (1.7%), flushing (1.1%), nausea (1%), and rash (1.1%).**

In addition, the following events were observed occasionally (less than 1%) in angina or hypertension trials:

**Cardiovascular**: Arrhythmias, AV block (second- or third-degree), bundle branch block, conduction defects, atrial fibrillation, atrial flutter, atrial tachycardia, atrial premature contractions.

**Central Nervous System**: Dizziness, drowsiness, edema, headache, hypotension, syncope, vertigo, paresthesias.

**Glaucoma**: Conjunctivitis, dry eye, tearing.

**Allergic Reactions**: Rash, pruritus, urticaria.

**Ocular**: Excessive tearing, photophobia.

**Respiratory**: Bronchospasm, cough, pharyngitis, pharyngolaryngitis, rhinitis, sinusitis.

**Others**: Anemia, chest pain, back pain, edema, fever, flu syndrome, gastrointestinal complaints, headache, hypertension, joint pain, lymphadenopathy, peripheral edema, phlebitis, pruritis, rash, sinusitis, vertigo.

**Laboratory**: Blood urea nitrogen, creatinine, electrolytes, gamma glutamyl transferase, glutathione peroxidase, glucose, hemoglobin, hematocrit, hemoglobin, iron, sodium, potassium, total protein, triglycerides, urinalysis.

**Cardiac**: Arrhythmia, atrial fibrillation, conduction defects, edema, hypertension, syncope, tachycardia, ventricular arrhythmia.

**Neuromuscular and Bone**: Arthralgia, myalgia, muscle spasm, pain, myasthenia gravis.

**Miscellaneous**: Abnormal AGT, AST, alkaline phosphatase, ALT, bilirubin, creatinine, FPG, GGT, hemoglobin, hematocrit, lymphocyte count, osmolality, potassium, sodium, total protein, triglycerides, urine sodium, uric acid, cholesterol, and triglycerides.

**Other**: Allergic reactions, chest pain, back pain, edema, fever, flu syndrome, gastrointestinal complaints, headache, hypertension, joint pain, lymphadenopathy, peripheral edema, phlebitis, pruritis, rash, sinusitis, vertigo.
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Diabetes Mellitus
Thyroid Disease
Parathyroid & Adrenal
Osteoporosis

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Headache & Back Pain
Dementia & Parkinson's
Peripheral Neuropathy

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Autoimmune Diseases
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New York Med. College
Robert A. Balk, M.D.
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University of Kentucky
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Rush Medical College
C. Rush, Joseph, M.D.
Rush Medical College
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As with other NSAIDs, the most frequent complaints are gastrointestinal, and rare hepatic and renal reactions have been reported.

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Once daily for comfort¹,²

Once daily for unsurpassed safety³,⁴,⁵

**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**

**Nasal Inhaler (triamcinolone acetonide)**

**FOR INTRanasal USE ONLY**

**SHAKE WELL BEFORE USING**

**BRIEF SUMMARY**

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

**WARNINGS:** The replacement of a systemic corticosteroid with a topical corticosteroid can be accomplished by signs of adrenal insufficiency and, in addition, some patients may experience symptoms of withdrawal, e.g., joint and/or muscular pain, lassitude and depression. Patients pretreated for prolonged periods with systemic corticosteroids and transferred to topical corticosteroids should be cautiously monitored for acute adrenal insufficiency in response to stress. In those patients who have asthma or other clinical conditions requiring long-term systemic corticosteroid treatment, systemic corticosteroids may in some cases exacerbate their symptoms.

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

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

**PRECAUTIONS**

General: In 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 topical 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 thrush showed absorption similar to that found in normal volunteers. Nasacort at 440 mcg/day for 42 days did not measurably affect adrenal response to a six-hour cosyntropin test. In the same studies (tripeptidyl) significantly reduced adrenal response to ACTH over the same period (see CLINICAL TRIALS section).

Nasacort Nasal Inhaler should be used with caution. If at all, in patients with active or quiescent tuberculous infections of the respiratory tract or in patients with untreated fungal, bacterial, or systemic viral infections or ocular herpes simplex.

Because of the inhibitory effect of corticosteroids on wound healing in patients who have experienced recent nasal septal ulcers, nasal surgery or trauma, a corticosteroid should be used with caution until healing has occurred.

When used at excessive doses, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, Nasacort Nasal Inhaler should be discontinued slowly, consistent with accepted procedures for discontinuing 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 steroid therapy and generally can be expected to occur within a few days of initiating therapy in allergic rhinitis. The patient should take the medication as directed and should not exceed the prescribed dosage. The patient should contact the physician if symptoms do not improve after three weeks, or if the condition worsens. Nasal irritation and/or burning or stinging after use of the spray occur only rarely with this product. The patient should contact the physician if 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, important to shake the canister well. Also, the canister should be discarded after 100 actuations.

**Cardiovascular:** Animal studies of triamcinolone acetonide to test its cardiogenic potential are underway.

**Impairment of Fertility:** Male and female rats which were administered oral triamcinolone acetonide at doses of 5 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 0.3 mg/kg/day (945 mcg/m2/day). However, a few female rats which received maternal toxicity doses of 8 or 15 mcg/kg/day (56 or 100 mcg/m2/day, respectively, as calculated on a surface area basis) exhibited cryptorchidism and prolonged delivery.

**Developmental toxicity, which included increases in fetal resorptions and stillbirths and decreases in pup body weight and survival, also occurred at the maternally toxic doses (0.5 and 1.0 mg/kg/day) and the same effect occurred at the same doses (1.0 and 2.0 mg/kg/day) when administered to pregnant rats.**

**Pregnancy:** Pregnancy Category C. Like other corticosteroids, triamcinolone acetonide has been shown to be teratogenic to rats and rabbits. Teratogenic effects, which occurred in both species at doses of 0.02, 0.04 and 0.08 mg/kg/day. The maximum human dose corresponded to 0.02, 0.04, 0.08, and 0.16 mg/kg/day in the rat and 320, 640 and 1280 mcg/m2/day in the rabbit as calculated on a surface area basis. However, these animal data are not necessarily predictive of drug-related adverse effects in humans.

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

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

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

**ADVERSE REACTIONS:** In clinical trials 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 spray. 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 820 days (average 332 days).

The most prevalent adverse experience was headache, being reported by approximately 18% of the patients who received Nasacort nasal spray. It was reported by 2.8% of the patients receiving Nasacort. Other nasal/mouth effects were reported by fewer than 5% of the patients who received Nasacort and included: dry mucous membranes, naso–sinus congestion, throat discomfort, sneezing, and epistaxis. The experiences do not usually interfere with treatment and, in the controlled and uncontrolled studies, approximately 1% of patients have discontinued because of these nasal adverse effects.

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

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

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

Please see product circular for full prescribing information.

**REFERENCES:**


Rhone Poulenc Rorer Pharmaceuticals Inc. 500 ARDILL ROAD, COLLEGEVILLE, PA 19426. 1.800.356.2599

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Cracks tough gram-negative cases*

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Millions of patients treated successfully worldwide over the past 7 years

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Please see brief summary of Prescribing information on last page of this advertisement.

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▲ Anxiolytic efficacy demonstrated in anxious patients with or without coexisting depressive symptoms.⁶

▲ Relief of anxiety symptoms begins within 1 week, progresses steadily through the fourth week of therapy.⁷

▲ Nonaddictive, no more sedation (10%) than seen with placebo (9%).⁸

▲ The more commonly observed untoward events include dizziness (12%), nausea (8%), headache (6%), and nervousness (5%).

Progressive Relief of Persistent Anxiety.

*BuSpar is not indicated for the relief of primary depressive disorder.

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**Topics will include**

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- Fraud and scientific misconduct
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The subject of the Congress is biomedical publication, but scholars in other disciplines are urged to participate, so that we may examine editorial peer review in the context of the overall scientific enterprise.

**For more information, contact**

Annette Flanagan, North American Coordinator, Peer Review Congress, JAMA, 515 N State St, Chicago, IL 60610; 312-464-2414, 312-464-5824 fax.

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See adjacent page for brief summary of prescribing information.
WARNINGS:
Acute cardiac I.V. bradycardia does not generally occur in patients on TENORMIN therapy. However, when severe bradycardia is observed in association with TENORMIN therapy, the patient should be closely observed and treatment limited to a single 25 mg dose while the patient is in a monitored hospital setting.

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In patients with systolic dysfunction, cardiac output may be impaired in response to the reduced myocardial contractility of TENORMIN. The effects of TENORMIN on cardiac output may cause severe hypotension in some patients. Therefore, TENORMIN should only be used in patients with normal cardiac output.

In the presence of hypovolemia, severe aortic stenosis, or severe mitral stenosis, the introduction of TENORMIN should be accompanied by close cardiac monitoring to guard against possible profound hypotension or bradycardia. The use of TENORMIN in patients with severe aortic stenosis should be done only in a clinical setting where invasively monitored cardiac output can be closely observed.

In patients with chronic obstructive pulmonary disease, TENORMIN should be used with caution, and with observation of respiratory function.

In Patients With Recent MI: Patients with a history of myocardial infarction (MI) should be observed closely when TENORMIN is introduced into therapy. Care must be taken in patients with left ventricular dysfunction, particularly those with a history of congestive heart failure.

Since TENORMIN has been shown to reduce the incidence of MI in patients with history of MI, in combination with other coronary care measures, TENORMIN has been used in patients with a history of MI.

In Patients with Previous Strokes: Patients with a history of stroke are at increased risk of recurrence, and should be closely observed. In patients with cerebrovascular disease, the introduction of TENORMIN should be done in a clinical setting where cardiac output can be closely monitored.

In Patients with Pheochromocytoma: In patients with pheochromocytoma, TENORMIN should only be used in a clinical setting where cardiac output can be closely monitored.

In Patients Undergoing Elective Surgery: TENORMIN should only be used in a clinical setting where cardiac output can be closely monitored.

In Patients Undergoing Digitalis Therapy: Digitalis glycosides are not routinely given to patients with heart failure who are being treated with TENORMIN. In patients given digitalis, severe hypotension may occur on the first dose of TENORMIN.

In Patients with Congestive Heart Failure: The introduction of TENORMIN in patients with congestive heart failure should be accompanied by close cardiac monitoring to guard against potentially profound hypotension or bradycardia.

In Patients with Limited Cardiac Reserve: TENORMIN should be used cautiously in patients with limited cardiac reserves.

In Patients with Mild Renal Impairment: TENORMIN is usually not associated with clinical signs of renal impairment. However, TENORMIN should be used with caution in patients with mild renal impairment (creatinine clearance of 30-50 ml/min).

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In Patients with Hepatic Impairment: TENORMIN is usually not associated with clinical signs of liver dysfunction. However, TENORMIN should be used with caution in patients with hepatic impairment.

In Patients with Pulmonary Hypertension: TENORMIN is usually not associated with clinical signs of pulmonary hypertension. However, TENORMIN should be used with caution in patients with pulmonary hypertension.

In Patients with History of Hypoglycemia: TENORMIN is not associated with an increased risk of hypoglycemia in patients with diabetes mellitus who are receiving TENORMIN. However, TENORMIN should be used with caution in patients with a history of hypoglycemia.

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In Patients with Early Pregnancy: The use of beta-blocking agents in early pregnancy has been shown to cause fetal abnormalities. Therefore, TENORMIN should not be used in early pregnancy.

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In Patients with Preterm Labor: TENORMIN is usually not associated with an increased risk of preterm labor.

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In Patients with Idiopathic Hypertension: TENORMIN is usually not associated with an increased risk of idiopathic hypertension.

In Patients with Hypertensive Crisis: TENORMIN is not associated with an increased risk of hypertensive crisis.

In Patients with Congestive Heart Failure: The introduction of TENORMIN in patients with congestive heart failure should be accompanied by close cardiac monitoring to guard against potentially profound hypotension or bradycardia.

In Patients with Myocardial Infarction: TENORMIN is usually not associated with an increased risk of myocardial infarction.

In Patients with Pericarditis: TENORMIN is not associated with an increased risk of pericarditis.

In Patients with Pericardial Effusion: TENORMIN is usually not associated with an increased risk of pericardial effusion.

In Patients with Diabetes Mellitus: TENORMIN is usually not associated with an increased risk of diabetes mellitus.

In Patients with Peptic Ulcer Disease: TENORMIN is not associated with an increased risk of peptic ulcer disease.

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In Patients with Basal Cell Carcinoma: TENORMIN is not associated with an increased risk of basal cell carcinoma.

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In Patients with Polycythemia Vera: TENORMIN is not associated with an increased risk of polycythemia vera.

In Patients with Cushing’s Syndrome: TENORMIN is not associated with an increased risk of Cushing’s syndrome.

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35 points to be considered in the differential diagnosis of hypokalemia as well as a clearly constructed flow diagram outlining the subsequent laboratory evaluation of this entity. In section 3, "Diseases of Organ Systems" (the most extensive part of the book), the text becomes appropriately academic, providing a synopsis of the laboratory manifestations of the most commonly presenting diseases. Pulmonary, gastrointestinal, renal, and endocrine disorders are but a few of the clinical areas addressed. Information in this section is also concisely presented, with each evaluation being covered in great depth. For example, in the case of a patient presenting with hepatic cirrhosis, Wallach reviews the expected findings, range of normal values, and variations for each hepatic function test available (eg, "serum LAP is slightly increased in 30% of patients, total serum cholesterol is normal or decreased"). After approaching cirrhosis generally, specific types (eg, Wilson's disease and hemochromatosis) are reviewed. Algorithms and tables abound, making the total format one that enhances both practitioners' knowledge of internal medicine and clinical efficiency in patient care. The last section, "Drugs and Laboratory Test Values," offers extremely useful tables that outline interactions of medications as reflected in results of laboratory tests. For "drugs that may cause increased urine catecholamines," 20 possible drug interactions are listed. The example of "drugs that can/may potentiate Coumarin action" shows how clinically relevant this section can be. A particular table in this section, "Drugs of Abuse," provided me with a new reference to street names, toxic levels, and appropriate assay of such drugs.

Above all, Wallach's index is the major asset of the manual. There are 130 pages of references to tests, conditions, diseases, symptoms, and medications that time after time send the reader exactly to where the desired information rests. The overwhelming thoroughness is demonstrated by the entry for sedimentation rate, which lists 70 areas of reference.

Interpretation of Diagnostic Tests continues to be so practical that it remains a "must have" for all clinical libraries. Students and residents alike will also continue to admire this manual, as it presents highly accessible essential laboratory information and decision-making advice relevant to both the learning process and preparation for examination in internal medicine. The trick with forthcoming editions is to keep this manual comprehensive while concise. Wallach continues as no other in capturing that goal.

James J. Bergman, MD
University of Washington
Seattle, Wash
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