Go ahead.
Take a good hard look.

PLENDIL stands up to serious scrutiny.
Consider efficacy. PLENDIL provides a
gradual onset of action for continuous 24-hour
blood pressure control in many hypertensive
patients. Alone or in combination with
another antihypertensive agent.

Consider suitability. PLENDIL is appro-
priate for a wide range of patients, including
many with concomitant disorders, such as:
hypercholesterolemia, diabetes, impaired
renal function, COPD, and asthma.

Consider safety. PLENDIL is generally
well tolerated when administered at recom-
mended dosages. Peripheral edema is the
most common unwanted effect.*

Consider dosage. The vast majority of
patients on PLENDIL receive prescriptions for
5 mg, once daily.¹

So go ahead and measure its worth.
Then give it serious consideration.

Plendil®
(felodipine) Tablets,
5 mg, 10 mg

Because you consider the whole patient.

* Peripheral edema is generally mild and age- and dose-related.
¹ 1993 IMS NPA Prescription Data.
PLENDIL is contraindicated in patients who are hypersensitive to this product.
Please see brief summary of Prescribing Information on page following
next page.
PRECAUTIONS

Gastric Ulcer: Patients with gastric ulcer should not be treated with PLENIDIL. It has been observed that some patients with gastric ulcer have an increased risk of developing gastric bleeding.

Neuroendocrine Tumors: Patients with neuroendocrine tumors should be treated with caution. It is recommended to monitor closely for signs of neuroendocrine tumor growth or progression.

Renal Function: PLENIDIL should be used with caution in patients with impaired renal function. Doses may need to be adjusted based on the patient's creatinine clearance.

CONTRAINDICATIONS

PLENIDIL is contraindicated in patients who are hypersensitive to this product.

Pregnancy

PLENIDIL is not recommended for use during pregnancy as there is no evidence of its safety for the mother and fetus.

Nursing Mothers

PLENIDIL is excreted in breast milk. Nursing mothers should be advised to discontinue breastfeeding while taking PLENIDIL.

Adverse Reactions

The most common adverse reactions associated with PLENIDIL include:

- Edema: Peripheral Edema, Cardiac Edema
- Hypotension
- Mucous Membrane Changes
- Nasal congestion
- Pruritus
- Hypersensitivity Reactions

Overdosage

In the event of an overdose, supportive and symptomatic care should be provided. The patient should be monitored for any signs of toxicity.

In addition, adverse reactions that occurred in up to 1.5% of patients who received PLENIDIL* in all controlled clinical studies (listed in order of decreasing severity within each category) and serious adverse events that occurred at a lower rate or were only found during marketing experience (those lower event rates are in italics) include:

- Body: As a Whole: Fatigue, warm sensation, Cough, Flushing
- Cardiovascular: Angina pectoris, arrhythmias, Bradycardia, chest pain, hypotension
- Dermatologic: Rash

In addition, the following adverse reaction has also been observed in patients treated with PLENIDIL:

- Gastrointestinal: Diarrhea

For more detailed information, consult your Astra Merck Specialist or see complete prescribing information.

Astra Merck Group of Merck & Co., Inc.
725 Chesterbrook Boulevard, Wayne, PA 19087

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**LOZOL® 1.25 mg once daily is now the recommended starting dose for indapamide in hypertension**

**LOW-DOSE ONCE-DAILY INDIAMPIRE TABLETS**

LOZOL®(indapamide) 1.25 mg and 2.5 mg tablets

BRAND NAME DRUGS

**INDICATION**: LOZOL (indapamide) is indicated for the treatment of hypertension alone or in combination with other antihypertensive drugs, and for the treatment of salt and fluid retention associated with congestive heart failure. Use in Pregnancy: See PRECAUTIONS.

**CONTRAINDICATIONS**: Anuria, hypersensitivity to indapamide or other sulfonamide drugs.

**WARNINGS**: Infrequent cases of severe hypokalemia, accompanied by hypokalemia, have been reported with 2.5 mg and 5.0 mg indapamide primarily in elderly females. Symptoms were reversed by electrolyte replenishment. Hypokalemia occurred possibly clinically significant (<125 mEq/L) has not been observed in clinical trials with the 1.25 mg dosage (see PRECAUTIONS). Hypokalemia occurs commonly with diuretics (see ADVERSE REACTIONS, hypokalemia), and electrolyte monitoring is essential. Generally, diuretics should not be given with lithium.

**PRECAUTIONS**: Periodic electrolyte determinations at appropriate intervals, especially in patients who are receiving diuretics or are receiving concurrent fluids, in patients subject to electrolyte imbalance, or in patients on a salt-restricted diet. In addition, patients should be observed for clinical signs of fluid or electrolyte imbalance, such as hypokalemia, hypocalcemia, dehydration, or hyponatremia. If the risk of hypokalemia secondary to diuretics and lithium is increased with larger doses, with a high degree of sodium loss, and with concurrent use of corticosteroids or ACTH. Intolerance with adequate dose reduction of diuretics may also contribute to hypokalemia. Hypokalemia can sensitize or exaggerate the response of the heart to the toxic effects of digitals, such as increased ventricular irritability. Diabetic hypokalemia may occur to edematous patients; appropriate treatment is usually water restriction. In actual salt depletion, appropriate replacement is the treatment of choice. Chloride deficit is usually mild; rating specific treatment except in extraordinary circumstances (renal, diabetic disease). Thiazide-like diuretics have been shown to increase the urinary excretion of magnesium, which may result in hypomagnesemia. Hypokalemia may occur, and frank goal may be predicated in certain patients receiving indapamide. Serum concentrations of chloride should be monitored periodically.

Use with caution in patients with severe renal disease; consider withholding or discontinuing if progressive renal impairment is observed. Renal function tests should be performed periodically.

Use with caution in patients with impaired hepatic function or progressive liver disease; since major alterations of fluid and electrolyte balance may precipitate hepatic coma.

* In patients with mild or moderate hypertension, a 4-week, single-blind placebo washout period was followed by an 8-week, open-label treatment period with LOZOL 2.5 mg. Patients responding to LOZOL 2.5 mg entered an 8-week, double-blind, randomized treatment period with either LOZOL 2.5 mg or LOZOL 1.25 mg. Treatment success was defined as a decrease in supine diastolic blood pressure to 90 mm Hg or less by week 8 of the double-blind period.

† Because of the diuretic effects of LOZOL 1.25, changes in certain electrolytes and blood chemistries can occur. Serum electrolytes and blood chemistries should therefore be monitored.

‡ 19.6% of patients had values less than 3.4 mg/L. Only 7.5% had potassium levels below 3.2 mEq/L and less than 1% fell below 3.0 mEq/L. Metabolic changes at higher doses of indapamide may be greater.

As in all step-down therapy, the patient should be monitored for maintenance of blood pressure control.

Please see brief summary of prescribing information below.

---

**LOZOL® (indapamide) 1.25 mg and 2.5 mg tablets**

BRAND NAME DRUGS

**INDICATION**: LOZOL (indapamide) is indicated for the treatment of hypertension alone or in combination with other antihypertensive drugs, and for the treatment of salt and fluid retention associated with congestive heart failure. Use in Pregnancy: See PRECAUTIONS.

**CONTRAINDICATIONS**: Anuria, hypersensitivity to indapamide or other sulfonamide drugs.

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As in all step-down therapy, the patient should be monitored for maintenance of blood pressure control.

Please see brief summary of prescribing information below.
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IN HYPERTENSION OR ANGINA

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(diltiazem HCl)

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ONCE A DAY
HEMODYNAMIC EFFECTS

In hypertension¹

• The magnitude of blood pressure reduction is related to the degree of hypertension

• Low incidence of vasodilatory side effects

• No reflex tachycardia is associated with chronic antihypertensive effects

In angina¹

• Potent dilator of coronary arteries* and reduces vasospasm

• Appropriate decrease in heart rate with a low incidence (<1%) of reflex tachycardia

• Little or no negative inotropic effect in patients with normal ventricular function†

WELL-TOLERATED CONTROL REGARDLESS OF AGE OR GENDER‡

• A side-effect discontinuation rate comparable to placebo in both hypertension and angina trials²

• Most commonly reported side effects are headache (5.4%), bradycardia (3.3%), first-degree AV block (3.3%), dizziness (3.0%), edema (2.6%), ECG abnormality (1.6%), and asthenia (1.8%)¹

* Demonstrated in patients with vasospastic angina.
† See Warnings and Clinical Pharmacology sections in prescribing information.
‡ In clinical trials with Cardizem CD.

Please see brief summary of prescribing information on next page.

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

FOR HYPERTENSION OR ANGINA

1122C4
ONCE-A-DAY CARDIZEM®
(diltiazem HCl)
120- 180-, 240-, 300-mg capsules
FOR HYPERTENSION OR ANGINA

Balf-Summary

Prescribing Information as of April 1993

CARDIZEM® CD
(diltiazem HCl)

Capsules

CONTRAINDICATIONS: CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular 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 80 mm Hg systolic), (4) patients who have demonstrated hypersensitivity to the drug, and (5) patients with acute myocardial infarction and pulmonary congestion due to left-sided heart failure, as a first-day administration. WARNINGS: 1. Cardiac Conduction. CARDIZEM 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 (20% of patients with 0% 90% of patients). Concomitant use of diltiazem with beta-blockers or digoxin may result in additive effects on cardiac conduction. A patient with Propranolol's angina developed periods of asystole (2 to 3 seconds) due to the combination of diltiazem and propranolol.

2. Congestive Heart Failure. Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (ejection). An acute study of oral diltiazem in patients with impaired ventricular function (ejection fraction 45% 6%) showed improvement in indices of ventricular function. However, prolonged treatment did not improve congestive heart failure. There have been reports in patients with worsening impairment of ventricular function. Experience with the use of CARDIZEM (diltiazem hydrochloride) in combination with beta-blockers in patients with impaired ventricular function is limited. CARDIZEM should be used with caution when using this combination.

3. Hypotension. Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.

4. Acute Hepatic Injury. Mild elevations of transaminases with and without concomitant elevation in alkaline phosphatase levels have been observed in clinical studies. Such elevations were usually transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, SGOT, SGPT, and other enzymes consistent with acute hepatic injury have been reported. These elevations tended to be asymptomatic and have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in some cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS: General: CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidney and in bile. As with all drug given over prolonged periods, laboratory tests of renal and hepatic function should be performed at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver that were reversible but which the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued therapy.

Dermatological events (see ADVERSE REACTIONS section) may be transient and may disappear despite continued use of CARDIZEM. However, skin reactions progressing to erythema multiforme and/or exfoliative dermatitis have been reported. In more than 2000 patients, only 18 had serious skin disorders. Given the potential for serious skin disorders, CARDIZEM should be discontinued if such reactions occur. In addition, patients should be cautioned to avoid exposure to strong sunlight during therapy.

Drug Interactions: Due to the potential for additive effects, caution and careful titration are warranted in patients receiving CARDIZEM concurrently with other agents known to affect cardiac conduction, and/or conduction. (See WARNINGS.) Pharmacokinetic studies indicate that the administration of diltiazem in prolonged AV conduction when using beta-blocking agents (see WARNINGS) and non-diltiazem calcium antagonists. As with all drugs, care should be exercised when treating patients with multiple medications. CARDIZEM undergoes biotransformation in the liver and is metabolized by the cytochrome P-450 mixed function oxidase enzyme system. Administration of CARDIZEM (diltiazem hydrochloride) concomitantly with propranolol in five normal volunteers resulted in increased propranolol levels in all subjects and bioavailability of propranolol was increased approximately 50%. In vitro, propranolol appears to be displaced from its binding sites by diltiazem. If combination therapy is initiated or withdrawn in combination with propranolol, an adjustment in the propranolol dose may be warranted. (See WARNINGS.)

Cimetidine: A study in six healthy volunteers has shown a significant increase in peak diltiazem plasma levels (128 ng/ml) following a 1-week course of cimetidine at 1200 mg per day and a single dose of diltiazem 80 mg. Ramilidine produced smaller, nonsignificant increases. The effect may be mediated by cimetidine's known inhibition of hepatic cytochrome P-450, the enzyme system responsible for the first-pass metabolism of diltiazem. Patients currently receiving diltiazem therapy should be carefully monitored for a change in pharmacological effect when initiating or discontinuing therapy with cimetidine. An adjustment in the diltiazem dose may be necessary. Digitoxin: Administration of CARDIZEM with digitoxin in 24 healthy male subjects increased plasma digitoxin concentration by 22% to 35% in both groups. Another investigator found no increase in digitoxin levels in 12 patients with coronary artery disease. Since there have been conflicting results regarding the effect of digitoxin levels, it is recommended that digitoxin levels be monitored when initiating, adjusting, and discontinuing CARDIZEM therapy to avoid possible over- or under-lowering. (See WARNINGS.)

Anesthetics: The depression of cardiac contractility, conductivity, and automaticity as well as the vasoactive action associated with digitalis-like agents may be potentitated by calcium channel blockers. When used concomitantly, anesthesiologists and calcium blockers should be titrated carefully.

Cyclosporine: A pharmacokinetic interaction between diltiazem and cyclosporine has been observed during studies involving renal and cardiac transplant patients. In renal and cardiac transplant recipients, a reduction of cyclosporine dose ranging from 15% to 40% was necessary to maintain cyclosporine trough concentrations similar to pre-transplant levels. In renal transplant recipients, it may be necessary to reduce the cyclosporine doses if concomitant administration of diltiazem is initiated. Close monitoring of cyclosporine levels is necessary when these drugs are administered concomitantly. Blood samples should be obtained 6-8 hours after cyclosporine administration for peak serum levels. Plasma concentrations of cyclosporine should be monitored 2-3 times and cyclosporine dose adjusted to maintain therapeutic levels. The effect of cyclosporine on diltiazem plasma concentrations has not been evaluated.

Carbamazepine: Concomitant administration of diltiazem with carbamazepine has been reported to result in elevated serum levels of carbamazepine (40% to 12% increase), resulting in toxicity in some patients. Patients receiving these drugs concurrently should be monitored for a potential drug interaction.

Carbohydrates, Malnutrition, Impairment of Fertility: A 24-month study in rats at oral dosages of up to 100 mg/kg/day and a 21-month study in mice at oral dosage levels of up to 30 mg/kg/day showed no evidence of carcinogenicity. There was also no mutagenic response in the Ames test, or in vivo in mammalian cell assays or in vitro in bacteria. No evidence of impaired fertility was observed in a study performed in male and female rats at oral dosages of up to 100 mg/kg/day.

Pregnancy: Animal Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was an increased incidence of stillbirths at doses of 20 times the human dose. There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Diltiazem is excreted in human milk. One report suggests that licking breast milk may approximate serum levels. If use of CARDIZEM 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 have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded from these studies. The following table presents the most common adverse reactions reported in placebo-controlled angina and hypertension trials in patients receiving CARDIZEM CD up to 390 mg with rates in placebo patients shown for comparison:

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Cardizem CD (n=607)</th>
<th>Placebo (n=301)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>6.4%</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>1.6%</td>
</tr>
<tr>
<td>JVP Block First Degree</td>
<td>3.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Edeema</td>
<td>2.6%</td>
<td>2.3%</td>
</tr>
<tr>
<td>ECG Abnormality</td>
<td>1.6%</td>
<td>1.7%</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 3900 patients, the most common events (i.e., greater than 1%) were edema (4%), headache (4%), dizziness (5%), asthenia (6%), first-degree AV block (2.4%), bradycardia (1.7%), flushing (1.4%), nausea (1.4%), and rash (1%). In addition, the following events were reported infrequently (less than 1%) in angina or hypertension trials: Cardiovascular: Angina, arrhythmia, AV block (second- or third-degree), bundle branch block, congestive heart failure, ECG abnormalities, hypotension, palpitations, syncope, tachycardia, ventricular extrasystoles. Respiratory: Abnormal dreams, anorexia, depression, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tremor, hiccups. Gastrointestinal: Anorexia, constipation, diarrhea, dry mouth, dyspepsia, dyspepsia, mild elevations of SGOT, SGPT, LDH, and alkaline phosphatase (see hepatic warnings), thirst, vomiting, weight increase. Urinary: Polyuria, proteinuria, pyuria. Other: Abdominal pain, dark urine, dysuria, epistaxis, eye irritation, hyperglycemia, hyperuricemia, impotence, muscle cramps, nasal congestion, itching, obstructive jaundice, polyuria, sexual difficulties. Other: Stomatitis, drug-induced immune reactions, rash, Steven's Johnson syndrome, drug-induced immune reactions, rash, Steven's Johnson syndrome. Patients receiving diltiazem therapy should be carefully monitored for a change in pharmacological action when initiating or discontinuing therapy with cimetidine. An adjustment in the diltiazem dose may be necessary. In patients with chronic renal failure, serum diltiazem concentrations were 1.4 to 2.3 times higher in patients with renal insufficiency than in patients with normal renal function. The effect of concomitant use of diltiazem on renal metabolism or elimination has not been defined. In patients with impaired renal function, diltiazem may accumulate to concentrations of 75 mg/ml or higher in some patients. (See WARNINGS.)

Health related problems are on our minds and in our news, affecting the way we live, the way we interact, the way we plan for our futures. They contribute to the amount of stress we face during the course of a normal day.

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**Key Note Speakers will include:**

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Michael F. Myers, MD, Department of Psychiatry, University of British Columbia speaking on the general conference theme from the Canadian perspective

**Other Speakers will include:**

Erica Frank, MD, on the Women Physicians Health Study

Joseph Newman, MD, on Disability due to Illness

James Winn, MD, on Physician Health and Medical Licensing Boards

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- Rapid response—substantial effect seen in as little as 1 to 3 nights of therapy\(^1\)
- A combined 15-year record of successful and safe use in the U.S. and Europe\(^2\)
- May be used hand in hand with behavior modification

Nighttime fluid intake should be restricted to decrease the potential occurrence of fluid overload; serum electrolytes should be checked at least once when therapy is continued beyond 7 days.

DDAVP\textsuperscript{®} Nasal Spray
(desmopressin acetate) 5mL

DRY NIGHTS FOR GOOD MORNINGS

Please see brief summary of prescribing information on adjacent page.