IN HYPERTENSION

When patients are difficult to manage...
It's time for TENORETIC.

Some hypertensive patients find it difficult to make dietary and life-style changes you recommend. Others simply don't respond to monotherapy. So continue to encourage a healthier life-style, and prescribe a simple, effective antihypertensive regimen for these patients. Initiate one-tablet-a-day TENORETIC therapy, the simplest regimen available. It works round the clock to lower blood pressure without added tablets or side effects that can so easily discourage compliance.

TENORETIC is not indicated for the initial therapy of hypertension. See adjacent page for brief summary of prescribing information.
What's a common denominator of most heart attack victims?

Mixed hyperlipidemias—elevated cholesterol and triglycerides—are common among heart attack victims, and nearly two-thirds of people who developed myocardial infarction in the PROCAM Trial had a low (<35 mg/dL) baseline level of HDL cholesterol.

HEART ATTACK PATIENTS (PROCAM TRIAL)

- HDL over 35 mg/dL: 36%
- HDL under 35 mg/dL: 64%
A powerful case for

LOPID®
BID

gemfibrozil
600-mg Tablets

Raised low HDL 25% —in patients whose baseline HDL was below 35 mg/dL in the landmark Helsinki Heart Study (HHS).³

Reduced heart attack incidence* up to 62% —in these HHS patients and 45% in HHS patients whose baseline HDL was below the median (46.4 mg/dL). Incidence of serious coronary events was similar for LOPID and placebo subgroups with baseline HDL above the median (46.4 mg/dL).³

Raised HDL levels 1½ to 3 times more effectively than lovastatin —in a 12-week, double-blind, randomized trial among patients with moderate to severe hyperlipidemia. Lovastatin achieved greater reductions in total serum cholesterol than gemfibrozil in this study population.⁴

RAISES HDL DRAMATICALLY REDUCES HEART ATTACK

LOPID is indicated for reducing the risk of coronary heart disease (CHD) in Type IIb patients with low HDL, in addition to elevated LDL and triglycerides, and who have had an inadequate response to weight loss, diet, exercise, and other pharmacologic agents such as bile acid sequestrants and nicotinic acid.

*Defined as a combination of definite coronary death and/or definite myocardial infarction.


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A powerful case for LOPID®

gemfibrozil

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RAISES HDL
DRAMATICALLY REDUCES HEART ATTACK

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Please see last page of this advertisement for warnings, contraindications, and brief summary of prescribing information.
**Lopid® (Gemfibrozil Capsules and Tablets)**

**Before prescribing, please see full prescribing information.**

A Brief Summary follows.

**CONTRAINDICATIONS.** 1. Hepatic or severe renal dysfunction, including primary biliary cirrhosis.

2. Preexisting gallbladder disease (See WARNINGS).

3. Hypersensitivity to gemfibrozil.

**WARNINGS.**

1. Because of the potential for gallbladder disease (See CONTRAINDICATIONS), the drug is withdrawn if lipid response is inadequate after 3 months of therapy. Efforts should be made to control serum lipids with appropriate diet, exercise and weight loss. Frequent prothrombin determinations are advisable until it has been definitely determined that adverse reactions that were more common among Lopid treatment group subjects but not statistically different from the excess of gallbladder surgery observed in the clofibrate group. This trend is consistent with the increased incidence of cholecystectomy observed in the main trial and in the 10-year follow-up study.
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Please see brief summary of Prescribing Information on next page.
Verapamil without the food variable

ENGINEERED WITH A NEW PATENTED* DELIVERY TECHNOLOGY FOR HYPERTENSION

New absorption profile
Controlled and predictable absorption over 24 hours with or without food.

Advanced convenience
With VERELAN, food intake is not required for consistent absorption. Traditional SR verapamil must be taken with food to achieve the desired absorption profile.

Advanced dosing simplicity
Once-a-day dosing for all dosages, even for patients requiring dosages over 240 mg a day.

NEW ONCE-A-DAY
VERELAN
VERAPAMIL HCl
PELLET-FILLED CAPSULES

120 mg
240 mg

Verapamil with food variables

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

US Patent Number 4,803,742
CalcanSR (G.D. Searle & Co), Ioxipam SR (Knoll Pharmaceuticals).

The usual dose is 240 mg once daily if adequate response and tolerance have been obtained. Higher doses of up to 360 mg or 480 mg once daily VERELAN 120 mg is available for patients requiring lower dose verapamil therapy.

WARNINGS

In patients with hepatic insufficiency, metabolism is delayed and half-life prolonged up to 10 to 20 times (see PRECAUTIONS). The retarded disposition is increased in patients with decreased renal function, resulting in about 30% of normal.

Cardiovascular: Severe LV dysfunction (see WARNINGS), hypotension (or systolic pressure < 90 mmHg), cardiogenic shock, sick sinus syndrome (if no pacemaker is present), second- or third-degree AV block (if no pacemaker is present), atrial flutter/atrial fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), or pre-excitation are contraindications (see 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 milder heart failure with optimum digitalization and diuretics before VERELAN is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported.

Several cases of hepatocellular injury have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving IV verapamil (or digoxin). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (second- and third-degree, O.8%). Development of marked first-degree block or progression to second- or third-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, second-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function (in 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 over dosage. 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 decrease verapamil dosage in patients with enhanced neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate. Atrophicventricular conduction and/or cardiac contractility, there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol clearance may occur with concomitant use. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Diuretics should not be given within 48 hours before or 24 hours after verapamil administration. Concurrent use of theodolol and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hyperlipidemic cardiomyopathy should be avoided, since significant hypotension may result. Verapamil has been given concurrently with short- and long-acting nitrates without any undesirable drug interactions. Interaction between cimelidine and chronically administered verapamil has not been studied. In healthy volunteers, clearance of verapamil was reduced or unchanged. Concurrent use of theodolol and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully.

Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Concurrent use of iron preparations and calcium antagonists need careful titration to avoid excessive cardiovascular depression. Verapamil may enhance the activity of neuromuscular blocking agents (curare-like and depolarizing), dosage reduction may be required. Atrial fib/atrial flutter/atrial fibrillation and a seconddegree or complete heart block may occur. Some studies noted that verapamil enhanced the antiarrhythmic properties of verapamil. Acute management:GENERAL: Mannitol 20 to 40 g IV, or 20% mannitol 100 to 200 mL IV over 1 hr, or intracranial pressure > 20 mmHg. SURGICAL: Benzyl penicillin 5 million units IV undiluted, or benzyl penicillin 5 million units IV undiluted and streptomycin 1 g IV undiluted, or aminoglycoside therapy. THERAPEUTIC: Furosemide 40 to 80 mg IV undiluted, or bumetanide 0.5 to 1 mg IV undiluted. DIGITALIS: Intravenous digoxin 0.5 to 1 mg IV undiluted, or intravenous digoxin 0.5 to 1 mg IV undiluted and furosamide 40 to 80 mg IV undiluted. DEPRESsorS: Propofol 2 to 4 mg/kg IV undiluted, or propofol 2 to 4 mg/kg IV undiluted and furosamide 40 to 80 mg IV undiluted. BLOOD: FFP 1 to 2 units, or FFP 1 to 2 units and platelets 1 to 2 units, or platelets 1 to 2 units and FFP 1 to 2 units. NONINVASIVE: Hyperventilation, head down, 100% oxygen, or 100% oxygen and invasive positive pressure ventilation. INVASIVE: Endotracheal intubation, mechanical ventilation, IABP, inotropic support, pressors, and/or CPR. SYSTEMIC: Epinephrine 2 to 3 mg IV undiluted, or epinephrine 2 to 3 mg IV undiluted and furosamide 40 to 80 mg IV undiluted. OTHER: Amiodarone 150 mg IV undiluted, or amiodarone 150 mg IV undiluted and furosamide 40 to 80 mg IV undiluted. MANUFACTURER: Lederle Laboratories DIVISION American Cyanamid Company. Pearl River, NY 10965

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**INDICATIONS AND USES:** TENORETIC is indicated in the treatment of hypertension. This fixed dose combination is intended to provide optimal antihypertensive therapy without limitation of dosage. If the fixed dose combination represents the dose appropriate to the individual patient's needs, it may be more convenient than the separate administration of the individual components.

**CONTRAINDICATIONS:** TENORETIC is contraindicated in patients with: sinus bradycardia; heart block greater than second degree; cardiogenic shock; severe hepatic or renal impairment; severe anemia; bradycardia; or symptomatic arterial hypotension. TENORETIC should not be used in patients requiring a high degree of bradycardia, such as those with atrial fibrillation or atrioventricular block.

**WARNINGS:**

- **Carotid Artery:** Symptomatic bradycardia may be associated with TENORETIC therapy, particularly in elderly patients. Patients with cardiac arrhythmias or other conditions predisposing to bradycardia are at increased risk. Bradycardia should be closely monitored in these patients.

- **Hypotension:** Hypotension may occur, particularly in the elderly, in patients with severe renal or hepatic impairment, or in those receiving concomitant use of agents that can cause hypotension.

- **Peripheral Vascular Disease:** Patients with peripheral vascular disease may experience exacerbations of angina.

- **Renal and Hepatic Disease:** Patients with renal or hepatic disease may experience exacerbations of angina.

- **Residual Lesions:** Residual lesions may be present following administration of TENORETIC.

- **Other Cardiovascular Disease:** Other cardiovascular disease may be present following administration of TENORETIC.

- **Cardiovascular Overload:** Cardiovascular overload may occur following administration of TENORETIC.

- **Other Cardiovascular Overload:** Other cardiovascular overload may occur following administration of TENORETIC.

- **Overdose:** Overdose may occur following administration of TENORETIC.

**ADVERSE REACTIONS:** TENORETIC is generally well tolerated. The most common adverse reactions associated with TENORETIC are headache, fatigue, nausea, dizziness, and cough.

**DOSAGE AND ADMINISTRATION:**

- **Antihypertensive Therapy:** The dosage of TENORETIC should be adjusted to the individual patient's needs. The recommended initial dose is 1 tablet (12.5 mg atenolol/25 mg chlorthalidone) daily. The dose may be increased at intervals of 1-2 weeks, if necessary, to achieve the desired response.

- **Renal and Hepatic Disease:** In patients with renal or hepatic disease, the dosage of TENORETIC should be reduced or the drug discontinued, as indicated.

- **Other Cardiovascular Disease:** Other cardiovascular disease may be present following administration of TENORETIC.

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