IN CERTAIN DYSLIPIDEMIAS

A Desirable Balance of Efficacy

LOPID® 300 mg
(gemfibrozil capsules, USP)

Lopid is indicated for treatment of adult patients with very high serum triglyceride levels in hyperlipoproteinemia other than type I who present a risk of pancreatitis and who do not respond adequately to diet.

© 1987 Warner-Lambert Company
with Patient Acceptance

**Efficacy** Lopid reduces synthesis\(^{1,3}\) and increases clearance of triglyceride-rich VLDL.\(^{2,3}\)

**Patient acceptance** Lopid has a very low order of side effects and has demonstrated limited effects on clinical and laboratory evaluations.\(^4\)

**Convenient BID dosage** Two 300-mg capsules taken 30 minutes before morning and evening meals help ensure patient compliance.

Diet, exercise, and weight loss are the first choice in therapy of lipid disorders.

**PARKE-DAVIS**

Please see next page for references and a brief summary of prescribing information.
Before prescribing, please see full prescribing information A Brief Summary follows.

CLINICAL PHARMACOLOGY. LOPID is a lipophilic agent which lowers elevated serum triglycerides primarily by reducing hepatic synthesis and release of very-low-density lipoprotein (VLDL) triglycerides. VLDL triglyceride levels were significantly decreased in clinic trials conducted in rats and mice at one and ten times the human dose. These decreases occur primarily in the very low density lipoprotein (VLDL) fraction and less frequently in the low density lipoprotein (LDL) fraction. It has been reported that the LDL in response to the administration of LOPID (50 to 1500 mg) daily is lower than normal, HDL, and LDL as well as apolipoproteins AI and AII. Epidemiological studies have shown that both low HDL cholesterol and high LDL cholesterol are independent risk factors for cardiovascular disease. Animal studies demonstrated that LOPID designates HDL cholesterol after morbidity or mortality due to coronary heart disease.

The mechanism of action has not been definitively established. In man, LOPID has been shown to inhibit or decrease lipoprotein lipase activity, thus reducing hepatic triglyceride production. LOPID inhibits synthesis and increases clearance of VLDL.carrier apoprotein B, leading to a decrease in VLDL production.

Animal studies suggested that LOPID may, in addition to slowing HDL cholesterol, reduce incorporation of long-chain fatty acids into newly formed triglycerides, accelerate turnover and removal of cholesterol from the liver, and increase excretion of cholesterol in the feces. LOPID is well absorbed from the gastrointestinal tract after oral administration. Plasma levels occur in one to two hours with a plasma half-life of 15 hours following multiple doses. Plasma levels appear proportional to dose and do not demonstrate accumulation across multiple doses.

LOPID mainly undergoes oxidation of a ring methyl group to successively form a hydroxyl and an aldehyde metabolite. Approximately 75% of the administered human dose is excreted in the urine, mostly as the glucuronide conjugate, with less than 2% excreted as unchanged gemfibrozil. Six percent of the dose is accounted for in the feces. In a clinical trial involving 427 patients, lipoprotein changes from average baseline (6%) by hyperlipoproteinemic (HLP) type are summarized below for these patients receiving gemfibrozil, 1200 mg/day, at the end of 12 weeks.

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INDICATIONS AND USAGE. The initial treatment for hypertriglyceridemia is dietary therapy specific for the type of hypertriglyceridemia. Drug therapy should not be used for the routine treatment of elevated levels for the prevention of coronary artery disease. Excess body weight and excess alcohol intake may be important factors in hypertriglyceridemia and should be addressed prior to any drug therapy. Physical exercise can be an important ancillary measure. Contributory diseases such as hyperthyroidism or diabetes mellitus should be looked for and adequately treated. The use of drugs should be considered only when reasonable attempts have been made to obtain satisfactory results with nondrug methods. If the decision to use drugs, the patient should be instructed that this does not reduce the importance of adhering to diet. Because of chemical, pharmacological, and clinical similarities between gemfibrozil and clofibrate, the adverse findings with clofibrate in two large clinical investigations (see Warnings) use of gemfibrozil should be restricted to the following indications.

LOPID may be considered for the treatment of adult patients with very high serum triglycerides (Type IIb or IV hyperlipoproteinemia) who present a risk of abdominal pain and pancreatitis and who do not respond adequately to a dietary effort to control them. Patients with triglyceride levels in excess of 750 mg per deciliter are likely to present such a risk. LOPID should be used on a weight-limited basis. Patients who need the most intensive measures of alimentary subjects have a more pronounced response. Therefore, the physician should be very selective and continue gemfibrozil treatment to patients with clearly defined risk due to severe hypertriglyceridemia (eg, individuals with familial hypercholesterolemia starting in childhood) who inadequately respond to appropriate diet and more effective cholesterol-lowering drugs. LOPID is not useful for the hypertriglyceridemia of Type I hyperlipidemia.

The biochemical response to gemfibrozil in patients is not consistent or positive to predict from the lipoprotein type or other factors which patients will obtain favorable results. It is essential that lipids be assessed and that the drug be discontinued after three months in any patient in whom lipids do not show significant improvement.

The effect of gemfibrozil-induced reduction of serum cholesterol or triglyceride levels or elevation of HDL cholesterol levels on morbidity or mortality due to coronary heart disease has not been established. Several years may be required before ongoing long-term investigations will resolve this question.

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

WARNINGS. 1. Because of chemical, pharmacological, and clinical similarities between gemfibrozil and clofibrate, the adverse findings with clofibrate in two large clinical investigations (see Warnings) use of gemfibrozil is not to be used for the routine treatment of elevated levels for the prevention of coronary artery disease. Excess body weight and excess alcohol intake may be important factors in hypertriglyceridemia and should be addressed prior to any drug therapy. Physical exercise can be an important ancillary measure. Contributory diseases such as hyperthyroidism or diabetes mellitus should be looked for and adequately treated. The use of drugs should be considered only when reasonable attempts have been made to obtain satisfactory results with nondrug methods. If the decision to use drugs, the patient should be instructed that this does not reduce the importance of adhering to diet. Because of chemical, pharmacological, and clinical similarities between gemfibrozil and clofibrate, the adverse findings with clofibrate in two large clinical investigations (see Warnings) use of gemfibrozil should be restricted to the following indications.

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Eighth International Symposium on Atherosclerosis
October 9-13, 1988
Rome

This symposium will include a review and update of basic science related to atherosclerosis and its complications in the fields of molecular biology and genetics; epidemiology; etiopathogenesis; lipoprotein metabolism and disorders; clinical and diagnostic aspects; dietary and drug treatment; and surgical treatment.

Satellite symposia to be held October 7-8 are Modified Lipoproteins (Venice), Hypertension and Atherosclerosis (Florence), and The Arterial Wall (Siena). Symposia to be held October 14-15 include Nutrition and Atherosclerosis (Capri), Epidemiology of Atherosclerosis (Porto Cervo), and Diabetes and Atherosclerosis (Ostuni).

The symposium is sponsored by the International Atherosclerosis Society. For additional information and registration, contact Dr G. Crepaldi, Symposium Chairman, c/o Organizing Secretariat, Centro Italiano Congressi, Via L. Spallanzani, 11, 00161 Rome, Italy. Telephone 06-864-155. Telex 622099 CIC I.
Vascular Cell Biology
Gordon Conference
Meriden, New Hampshire
July 31–August 6, 1988

This will be the first of a semiannual series devoted to cellular and molecular biology of blood vessels. Major topics will include developmental biology, neurovascular biology, signaling within the vessel wall, vascular immunology, and vascular enzymology.
Invalidation to register will be published in Science. Priority will be given to individuals interested in submitting new data at the poster session or participating as discussants.

For additional information, write:
Stephen M. Schwartz, MD, PhD
Department of Pathology, SJ-60
University of Washington
Seattle, WA 98195

or
Paul DiCorleto, PhD
Research Division
Cleveland Clinic Foundation
9500 Euclid Avenue
Cleveland, OH 44106

1988 Aspen Hepatic Cholesterol and Lipoprotein Conference
Given Institute of Pathobiology, Aspen, Colorado
August 18–21, 1988

A research conference on regulation of cholesterol and bile acid biosynthesis, the role of the liver in lipoprotein uptake and biosynthesis, and the role of fatty acid binding proteins will be held August 18–21, 1988, in Aspen, Colorado. Topics include current research on hepatic lipoprotein receptors, lipoprotein biogenesis, and intracellular lipid transport.

Cochairmen of the conference are Peter A. Edwards, Division of Cardiology and Department of Biological Chemistry, UCLA School of Medicine, Los Angeles, CA 90024, and Scott M. Grundy, Center for Human Nutrition, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd, Dallas, TX 75235.

Limited funds are available to sponsor students, research fellows, postdoctoral trainees, and young faculty. Interested individuals should send a curriculum vitae and a short abstract to Dr Peter A. Edwards at the address above.

In addition, some opportunities are available for investigators to attend for a small fee to cover expenses. All participants are invited to submit abstracts for poster presentations.

The deadline for receipt of applications is May 18, 1988.
American Heart Association
National Research Program

Medical Student Research Fellowship
1989-1990

Institutional award to encourage medical students to engage in full-time research training for one or more years prior to graduation.

Application Deadline
Receipt June 1, 1988
for award activation July, 1989

Information:
Division of Research Administration
American Heart Association
7320 Greenville Avenue
Dallas, Texas 75231
(214) 706-1453

Participation by qualified minority candidates is encouraged

American Heart Association
National Research Program

Clinician Scientist Award
1989-1990

To encourage promising clinically trained physicians to undertake careers in investigative science.

Application Deadline
Receipt June 1, 1988
for award activation July, 1989

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Division of Research Administration
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