When he's not coughing, is his antibiotic making him queasy?
Bronchitis is difficult enough without the nausea that may sometimes accompany doxycycline therapy. The pellets of DORYX, however, pass intact through the stomach and dissolve in the small intestine—reducing the potential for GI upset and nausea while providing all the benefits of doxycycline.\(^1\)

<table>
<thead>
<tr>
<th>Mean Nausea Scores as Reported by Subjects*1</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLACEBO 0.7</td>
</tr>
<tr>
<td>DORYX* (coated doxycycline hyclate pellets) 1.6</td>
</tr>
<tr>
<td>VIBRAMYCIN® Hyclate (doxycycline hyclate) 3.2</td>
</tr>
</tbody>
</table>

The doxycycline in DORYX is active against such respiratory pathogens as *Streptococcus pneumoniae*,\(^2\) *Hemophilus influenzae*,\(^2\) *Mycoplasma pneumoniae*,\(^3\) and *Chlamydia psittaci*.\(^4\)

**Once-a-day dosing**

DORYX gives your bronchitis\(^\ddagger\) patients the convenience of once-a-day dosing, to promote compliance. And DORYX may be taken with meals.

Switch to DORYX. For efficacy with excellent tolerability.

\(^\ddagger\)Due to susceptible organisms.

**Doxycycline with a difference.**

**DORYX® Pellets**

(coated doxycycline hyclate pellets) 100-mg Capsules

PARKE-DAVIS
Please see next page for brief summary of prescribing information.
DORYX® Pellets (coated doxycycline hyclate pellets) 100-mg capsules

DORYX® (coated doxycycline hyclate pellets)

Before prescribing, please see full prescribing information. A Brief Summary follows.

INDICATIONS AND USAGE. Doxycycline is indicated in infections caused by the following microorganisms:

- Rocky Mountain spotted fever, typhus fever and the typhus group: O. lepeticus, tick-borne typhus fever, and louse-borne typhus fever
- Atypical Mycobacteria
- The spirochete agent of syphilis and other spirochetal infections (Rickettsiae (Rocky Mountain spotted fever, Q fever, and the typhus group), Treponema pallidum (syphilis and yaws), and Oroya fever
- Endemic granulomatous trachoma
- Streptococcal infections, therapy should be continued for at least 10 days

Laboratory tests: In venereal disease when coexistent syphilis is suspected, dark-field examination should be done before treatment is started and the blood serology repeated monthly for at least 4 months.

In long-term therapy, periodic laboratory evaluation of organ systems, including hematopoietic, renal, and hepatic studies may be necessary.

Drug interactions: Because tetracyclines have been shown to depress plasma prothrombin activity in patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracyclines in conjunction with penicillin.

For concomitant therapy with antiradicines or anticoagulant preparations and food see "Dosage and Administration" section.

Carelessness, mutagenesis, interruption of fertility: Long-term studies are currently being conducted to determine whether tetracyclines have carcinogenic potential. Animal studies conducted in rats and mice have not provided conclusive evidence that tetracyclines may be carcinogenic or that they induce tumors. In two mammalian cell assay systems (LS1784 mouse lymphoma and Chinese hamster lung cells in vitro) positive responses for mutagenicity occurred at concentrations of 50 and 100 μg/ml, respectively. In human no association between tetracyclines and these effects have been made.

Pregnancy: Pregnancy Category D (See Warnings section).

Nursing Mothers: Tetracyclines are present in the milk of lactating women who are taking a drug in this class. Because of the potential for serious adverse reactions in nursing infants from the tetracyclines, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother (see Warnings section).

Pediatric Use: See Warnings and Dosage and Administration sections.

ADVERSE REACTIONS. Due to oral tetracyclines virtually complete absorption, side effects to the lower bowel, particularly diarrhea, have been infrequent. The following adverse reactions have been observed in patients receiving tetracyclines.

Gastrointestinal: Anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, and inflammatory lesions (with monilial overgrowth) in the anogenital region. These reactions have been reported with both the oral and parenteral administration of tetracyclines. Rare instances of esophagitis and esophageal ulcerations have been reported in patients receiving capsules and tablet forms of drugs in the tetracycline class. Most of these patients took more than 1 gram of tetracycline per day for a week or more. Skin: Maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Photosensitivity is discussed above (See Warnings).

Reno-vascular: Rise in BUN has been reported and is dose related. (See Warnings).

Hypersensitivity reactions: Urticaria, angioneurotic edema, anaphylaxis, arthropod purpura, pemphigus, and exacerbation of systemic lupus erythematosus.

Bulging fontanelles in infants and benign intracranial hypertension in adults have been reported in individuals receiving tetracyclines. These conditions disappeared when the drug was discontinued.

Blood: Hemolytic anemia, thrombocytopenia, neutropenia, and eosinophilia have been reported with tetracyclines.

When given over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands. No abnormalities of thyroid function are known.

DOSE AND ADMINISTRATION. The usual dosage and frequency of administration of doxycycline differs from that of the other tetracyclines exceeding the recommended dosage may result in an increased incidence of side effects.

The usual adult dose of tetracycline is 200 mg on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg/day. The maintenance dose may be administered as a single dose or 50 mg every 12 hours. In the management of more severe infections (particularly chronic infecstions of the urinary tract), 100 mg every 12 hours is recommended.

In children above eight years of age, the recommended dosage schedule for children weighing 100 pounds or less is 2/3 to 2 mg/lb of body weight divided into two doses on the first day of treatment, followed by one mg/lb of body weight given as a single daily dose or divided into two doses on subsequent days. For more severe initial administration of tetracyclines, 2 mg/lb of body weight may be used. For children over 100 pounds, the usual adult dose should be used.

Uncomplicated gonococcal infections in adults (except anorectal infections) caused by C. trachomatis and N. gonorrhoeae. The usual adult dose of tetracycline is 200 mg stat followed in one hour by a second 300 mg dose. The dose may be administered with food, including milk or carbonated beverages; however, evidence that tetracyclines are absorbed equally when administered with or without food has been obtained. Acidic edoxymyocytes caused by N. gonorrhoeae: 100 mg by mouth, twice a day for at least 10 days.

Penicillinase-resistant gonococcal infections, acute syphilis, and pelvic inflammatory disease in adults caused by C. trachomatis. The usual adult dose of tetracycline is 200 mg stat followed one hour by a second 300 mg dose. The dose may be administered with food, including milk or carbonated beverages; however, evidence that tetracyclines are absorbed equally when administered with or without food has been obtained. Acidic edoxymyocytes caused by C. trachomatis: 100 mg by mouth, twice a day for at least 7 days.

Acute pelvic inflammatory disease caused by C. trachomatis: 100 mg by mouth, twice a day for at least 7 days.

Acute pelvic inflammatory disease caused by N. gonorrhoeae: 100 mg by mouth, twice a day for at least 7 days.

The therapeutic antibacterial serum activity usually persists for 24 hours following recommended dosage.

When used in streptococcal infections, therapy should be continued for 10 days.

Administration of adequate amounts of fluid along with capsules and tablet forms of drugs in the tetracycline class is recommended to reduce the risk of esophageal irritation and ulceration (see Adverse Reactions).

If gastric irritation occurs, it is recommended that the drug be given with food or milk. The absence of doxycycline is not markedly influenced by simultaneous ingestion of food or milk.

Concomitant therapy: Antacids containing aluminum, calcium, or magnesium, sodium bicarbonate, and iron-containing preparations should not be given to patients taking oral tetracyclines.

Studies to date have indicated that administration of doxycycline at the usual recommended dose does not lead to excessive accumulation of the antibiotic in patients with renal impairment.

Caution—Federai law prohibits dispensing without prescription.

References


Doxycycline hyclate pellets) of doxycycline hyclate pellets) were packaged into transferable aerosol containers.

Manufactured by

Printed International

2425700134

Distributed by

Division of Warner Lambert Company

Mans Plain, New Jersey 07950

PO 5S J5 504 P(12 68)
ANNOUNCEMENT AND CALL FOR PAPERS
IV INTERNATIONAL MEETING OF FAMILY MEDICINE
FOR THE AMERICAS, SPAIN, AND PORTUGAL

"THE CHALLENGE OF QUALITY"
ESTORIL, PORTUGAL
May 24-26, 1990

Registration fees are as follows:

• Active Members ICFM $100
• Nonmembers ICFM $200

Guidelines for the Submission of Abstracts:

Free Papers:

• The entire abstract (200 words) should include title, authors, institution, and country.
  Abstracts can be typed in Portuguese, English, or Spanish.

• The abstract should be as informative as possible:
  a) state the specific objective of the study
  b) describe methods used, if pertinent
  c) summarize results obtained
  d) state conclusions reached

• Abstracts should be typed carefully and clearly. Only standard abbreviations may be used.

• Abstracts will be reproduced in the Volume of Abstracts EXACTLY AS SUBMITTED. Please avoid corrections, smudges, errors, and misspellings.

• Airmail abstract and 3 copies to:

IV INTERNATIONAL MEETING PAPER SUBMISSION

c/o Nicholas J. Pisacano, M.D.
American Board of Family Practice
2228 Young Drive
Lexington, Kentucky 40503
USA

DEADLINE FOR RECEIPT OF ABSTRACTS IS JANUARY 31, 1990

Organized by: The Portuguese Association of General Practitioners
Sponsored by: The International Center for Family Medicine and The Society of Teachers of Family Medicine
It's never been more important to specify 'Dyazide'.
Because that's the only way you can be sure your patients will receive 'Dyazide' quality...the quality that physicians and their patients have trusted for 25 years.

'Dyazide'—prescribe it with confidence, prescribe it by name. Specify, “Dispense as Written.” Ask your patients to make sure that's what they receive when they present your prescription.

*There is no bioequivalent generic substitute for 'Dyazide'.

It's never been more important.

The unique red and white Dyazide® capsule:
Your assurance of SK&F quality.

a product of
SK&F LAB CO.
Cidra, P.R. 00639 © SK&F Lab Co., 1989
IN UTI

WHAT YOU NEED

A PROVEN HIGH DEGREE OF EFFICACY
BROAD UTI SPECTRUM

For a Brief Summary of Prescribing Information, please see the last page of this advertisement.
WHERE YOU NEED IT

High concentrations in the urinary tract exceed the MIC$_{90}$ of most uropathogens by 100-fold

NOROXIN* (Norfloxacain, MSD) is contraindicated in patients with a history of hypersensitivity to norfloxacain or the quinolone group of antibacterial agents (e.g., nalidixic acid and cinoxacin).

Norfloxacain should not be used in children or pregnant women.

Patients should be advised to take NOROXIN one hour before or two hours after a meal. Patients should also be advised to drink fluids liberally and not to take antacids concomitantly or within two hours after dosing.

For a Brief Summary of Prescribing Information, please see the last page of this advertisement.
FOR MANY UTI PATIENTS

ALL YOU NEED

NOROXIN®

(TABLETS)

NORFLOXACIN | MSD

THE UTI SPECIALIST

- Highly effective in clinical trials: 95% cured or improved*
- High degree of aerobe specificity
- Broader UTI spectrum than many oral and parenteral agents
- Generally well tolerated; convenient b.i.d. dosage

*88% cured, 7% improved
Cured: elimination of clinical signs, symptoms, and infecting organism(s).
Improved: eradication of infecting organism(s) with decrease in clinical signs and symptoms.
WHAT YOU NEED WHERE YOU NEED IT ALL YOU NEED FOR MANY UTI PATIENTS

NOROXIN® (NORFLOXACIN | MSD)
THE UTI SPECIALIST

DESCRIPTION: NOROXIN® (Norfloxacin, MSD) is a synthetic, broad-spectrum antibacterial agent for oral administration. Norfloxacin, a fluoroquinolone, is 1-ethyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolineracetic acid and differs from quinolones by having a fluoro atom at the 6 position and a piperazine moiety at the 7 position.

INDICATIONS AND USAGE: NOROXIN® is indicated for the treatment of adults with complicated and uncomplicated urinary tract infections that are caused by susceptible strains of the designated microorganisms listed below:

- Escherichia coli
- Klebsiella pneumoniae
- Enterobacter cloacae
- Proteus mirabilis
- indole positive Proteus species
- Providencia rettgeri
- Morganella morganii
- Pseudomonas aeruginosa
- Citrobacter freundii
- Staphylococcus aureus
- Staphylococcus epidermidis

Note: Specimens for culture and susceptibility testing should be obtained prior to and during treatment if clinical response warrants. However, NOROXIN® may be used to initiate therapy in urinary tract infections prior to the availability of laboratory results.

CONTRAINDICATIONS: NOROXIN® is contraindicated in patients with a history of hypersensitivity to norfloxacin or the quinolone group of antibacterial agents (e.g., nalidixic acid and cinoxacin).

WARNINGS: Norfloxacin should not be used in children or pregnant women.

The oral administration of single doses of norfloxacin, 6 times the recommended human clinical dose, caused lameness in immature dogs. Histologic examination of the weight-bearing joints of these dogs revealed permanent lesions of the cartilage. Related drugs (e.g., nalidixic acid and cinoxacin) are associated with erosions of the cartilage in weight-bearing joints and other signs of arthropathy in immature animals of various species.

PRECAUTIONS: Needle shaped crystals were found in the urine of some volunteers who received either placebo, 360 mg norfloxacin, or 1600 mg norfloxacin (at or twice the recommended daily dose, respectively) while participating in a double-blind, crossover study comparing single doses of norfloxacin with placebo. While crystalluria is not expected to occur under usual conditions with a dosage regimen of 400 mg b.i.d., a precaution, the daily recommended dosage should not be exceeded and the patient should drink sufficient fluids to ensure a proper state of hydration and adequate urinary output.

Alopecia in dogs has been reported with norfloxacin although no causal relationship has been established. Convolusions, increased intracranial pressure, and toxic psychoses have been reported with other drugs in this class. If these reactions occur in patients receiving norfloxacin, the drug should be discontinued and appropriate measures instituted. The effects of norfloxacin on brain function or on the electrical activity of the brain have not been tested. Until more information becomes available, quinolones should be used with caution in patients with known factors which predispose to seizures.

Drug Interactions: Diminished urinary excretion of norfloxacin has been reported during the concomitant administration of probenecid and norfloxacin.

The concomitant use of nitrofurantoin is not recommended since nitrofurantoin may antagonize the antibacterial effect of NOROXIN® (Norfloxacin, MSD) in the urinary tract.

The concomitant administration of norfloxacin with antacids is not recommended.

Information for Patients: Patients should be advised to take NOROXIN® one hour before or two hours after a meal. Patients should also be advised to drink fluids liberally and not to take antacids concomitantly or within two hours after dosing.

NOROXIN® may cause dizziness or lightheadedness; therefore, patients should know how they react to norfloxacin before they operate an automobile or machinery or engage in activities requiring mental alertness and coordination.

Pregnancy: Pregnancy Category C: Norfloxacin has been shown to produce embryonic loss in monkeys when given in doses 10 times the maximum human dose (400 mg b.i.d.), with peak plasma levels that are 2 to 3 times those obtained in humans. There has been no evidence of a teratogenic effect in any of the animal species tested (rat, rabbit, mouse, monkey) at 5-30 times the human dose. There were no adequate and well controlled studies in pregnant women. Since norfloxacin, like other drugs in this class, causes arthropathy in immature animals, it should not be used in pregnant women (see WARNINGS).

Nursing Mothers: It is not known whether norfloxacin is excreted in human milk.

When a 200 mg dose of NOROXIN® was administered to nursing mothers, norfloxacin was not detected in human milk. However, because the dose studied was low, because other drugs in this class are secreted in human milk, and because of the potential for serious adverse reactions from norfloxacin in nursing infants, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Norfloxacin should not be used in children because it causes arthropathy in juvenile animals (see WARNINGS).

ADVERSE REACTIONS: In clinical trials, NOROXIN® was generally well tolerated.

The incidence of subjects reporting drug related adverse experiences in clinical trials involving 1127 subjects was 3.4%. However, the incidence figures below were calculated without reference to the indication.

The most common adverse experiences (1%-3%) were either:

- Abdominal pain, dyspepsia, nausea, vomiting, diarrhea, and dysentery
- White blood cell count, erythema, and pruritus
- Fatigue
- Rash, pruritus, and exfoliative dermatitis

Additional reactions (0.3%-1%) were:

- Vomiting
- Headache
- Rash

Less frequent reactions included:

- Dry mouth, diarrhoea, fever, somnolence, and asthenia

CNS effects characterized as generalized seizures and myoclonus have been reported rarely with NOROXIN®. A causal relationship with NOROXIN® has not been established (see PRECAUTIONS).

Visual disturbances have been reported with drugs in this class.

Abnormal laboratory values observed in these 1127 subjects in clinical trials were eosinophilia 1.8%, elevation of ALT (3xULN) and AST (3xULN) 1.8%, increased alkaline phosphatase 1.4%, and decreased WBC or neutrophil count 1.2%. Those occurring less frequently included increased BUN, serum creatinine, and LDH, and decreased hematocrit.

The following additional adverse reactions have been reported since the drug was marketed:

Hypersensitivity Reactions: Hypersensitivity reactions have been reported including anaphylactic reactions, angioedema, urticaria, anaesthesia, and angioedema. Skin: Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythematous dermatitis, photosensitivity. Gastrointestinal: Pseudomembranous colitis. Nervous System/Psychiatric: Psychotic disturbances including psychic reactions and confusion, paresthesia.

Hematologic: Neutropenia, leukopenia, thrombocytopenia.

DOSAGE AND ADMINISTRATION: NOROXIN® (Norfloxacin, MSD) should be taken one hour before or two hours after a meal with a glass of water. Patients receiving NOROXIN® should be well hydrated (see PRECAUTIONS).

Normal Renal Function: The recommended dosage of NOROXIN® is:

- Uncomplicated urinary tract infections: 400 mg twice daily for 7 to 10 days. Complicated urinary tract infections: 400 mg twice daily for 10 to 21 days. Maximum total daily dosage should not exceed 800 mg per day.

Renal Impairment: NOROXIN® may be used for the treatment of urinary tract infections in patients with renal insufficiency. Although patients with a creatinine clearance rate of 30 mL/min.1.73m2 or less, the recommended dosage is one 400 mg tablet once daily for the duration given above. At this dosage, the urinary concentration exceeds the MICs for most urinary pathogens susceptible to norfloxacin. When the urinary creatinine clearance is less than 10 mL/min.1.73m2:

- When only the serum creatinine level is available, the following formula (based on sex, weight, and age of the patient) may be used to convert this value into creatinine clearance. The serum creatinine should represent a steady state of renal function.

  
  Males: = (weight in kg) x (140 - age) / (72) x serum creatinine (mg/100 mL)

  Females: = (0.85 x (above value))

Elderly: Elderly patients with a creatinine clearance of greater than 30 mL/min.1.73m2 should receive the dosages recommended under Normal Renal Function.

Elderly patients with a creatinine clearance of 30 mL/min.1.73m2 or less should receive 400 mg once daily as recommended under Renal Impairment.

HOW SUPPLIED: Dark pink, oval shaped, film-coated tablets, coded MSD 750 on one side and NOROXIN on the other, in bottles of 100, unit-of-use bottles of 30, and unit-dose packages of 100.

For more detailed information, consult your MSD Representative or see Prescribing Information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19486.
Hypertension control that doesn't disturb the delicate balance of the individual.

ONCE DAILY*

ISOPTIN<sup>SR</sup>

(VERAPAMIL HCl) 240mg

Sustained-Release Tablets

Effective monotherapy that respects the individual profiles of more patient types.<sup>1,2</sup>

*Consult Dosage and Administration section of the package insert for full prescribing information. Please see brief summary on reverse side for safety information.
First line anti-hypertensive therapy for more patient types.

- Low incidence of fatigue.
- Low incidence of depression.
- Impotence rarely reported.
- No changes seen in the renin-angiotensin-aldosterone system.\(^1\,\text{,}^4\)
- Particularly effective in patients with low renin levels.\(^3\)
- No adverse effect on serum potassium, uric acid or blood glucose levels.\(^5\,\text{,}^6\)
- Does not increase serum cholesterol or triglycerides.\(^7\,\text{,}^8\)

\(^1\) \(^4\) \(^3\) \(^5\) \(^6\) \(^7\) \(^8\)

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

**WARNINGS:**
Heart Failure: ISOPTN should be avoided in patients with severe left ventricular dysfunction. Patients with mild ventricular dysfunction should, if possible, be controlled before verapamil treatment. ISOPTN should be avoided in patients with any degree of left ventricular dysfunction if they are receiving a beta adrenergic blocker (see DRUG INTERACTIONS). Hypotension: ISOPTIN (verapamil HCl) may produce clinical symptoms of severe hypotension. Elevations of transaminases with and without concomitant 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 a coexisting accessory AV pathway may develop increased antegrade conduction across the accessory pathway producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous verapamil. While this has not been reported with oral verapamil, it should be considered a potential risk (see Contraindications). Treatment is usually D.C. cardioversion. Atrioventricular Block: The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1st degree AV block and transient bradycardia. Higher degrees of AV block and complete AV heart block have been infrequent (0.9%) and have been associated with a reduction in dosage or in rare instances, discontinua-
tion of verapamil HCl. Patients with Hypertrophic Cardiomyopathy (HCH): Although verapamil has been used in the therapy of patients with HCH, severe cardiovascular decompensation and death have been noted in this patient population.

**PRECAUTIONS:**
Impaired Hepatic or Renal Function: Verapamil is highly metabolized by the liver with greater than 70% of an administered dose excreted as metabolites in the urine. In patients with impaired hepatic function the dose should be cut to 30% of the usual dose and the patient closely monitored. In patients with impaired renal function verapamil should be administered cautiously and the patients monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see Overdose). Use in Patients with Alternated (Decreased) Neuromuscular Transmission: Verapamil decreases neuromuscular transmission and may prolong recovery from neuromuscular blocking agents. In patients with attenuated neuromuscular transmission lower doses of verapamil may be warranted.

Drug Interactions: Beta Blockers: Concomitant use of ISOPTN and oral beta-adrenergic blocking agents may result in additive negative effects on heart rate, atrioventricular conduction, and/or car-
diac contractility. Excessive bradycardia and AV block has been reported. The combination should be used only with caution and close monitoring. Digitalis: Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated. However, chronic verapamil treatment increases serum digoxin levels by 50% to 75% during the first 24 hours of therapy and this can result in digitalis toxicity. Upon discontinuation of ISOPTN (verapamil HCl), the patient should be reassessed to avoid unmasking digitalis toxicity. Antihypertensive Agents: Verapamil administered concomitantly with oral antihy-
pertensive agents (e.g., vasodilators, angiotensin-converting enzyme inhibitors, diuretics, alpha and beta adrenergic blockers) will usually have an additive effect on lowering blood pressure. Patients receiving these combinations should be appropriately monitored. Antihypertensive Agents: Diisopropamide: Diisopropamide should not be administered within 48 hours before or 24 hours after verapamil administration. Flunarizine: Concomitant administration of flunarizine and verapamil may result in additive negative inotropic effect and prolongation of atrioventricular conduction. Quinidine: In patients with hypertrophic cardiomyopathy (HCH), concomitant use of verapamil and quinidine may result in significant hypotension. Other: Nitrates: The pharmacological profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions. Cimetidine: Variable results on clearance have been obtained in acute studies of healthy volunteers; clearance of verapamil was either reduced or unchanged. Lithium: Pharmacokinetic (lowering of serum lithium levels) and pharmacodynamic (increased sensitivity to the effects of lithium) interactions between oral verapamil and lithium have been reported. Carbamazepine: Verapamil therapy may increase carbamazepine concentra-
tions and produce related side effects during combined therapy. Ritalin: Therapy with
What's a common denominator of most heart attack victims?
HDL

<35

mg/dL

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.
A powerful case for

LOPID®<sup>BID</sup>

(gemfibrozil)<sup>600-mg Tablets</sup>

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

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).<sup>3</sup>

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.<sup>4</sup>

**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.


Please see last page of this advertisement for warnings, contraindications, and brief summary of prescribing information.
Lipid® (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).

WARNING: Significant clinical, pharmacological, and clinical similarities between gemfibrozil and clofibrate, the adverse findings with clofibrate in two large clinical studies may also apply to gemfibrozil. In the first of those studies, the Coronary Drug Project (CDP), 386 patients with angina pectoris and after treatment in the second, the Helsinki Heart Study. The Helsinki Heart Study discontinue treatment with clofibrate. There was no difference in mortality between the clofibrate-treated subjects and 3000 placebo-treated subjects, but twice as many clofibrate-treated subjects died of myocardial infarction than did the placebo-treated group. A trial of clofibrate was conducted by the World Health Organization (WHO), 5000 subjects without known coronary heart disease were treated with clofibrate for five years and followed one year thereafter. The excess mortality was significantly different from the 29% excess mortality seen in the clofibrate group in the separate WHO study. Noncoronary heart disease related mortality showed a similar trend in the Lipid (43% vs. 27% in the placebo group). In the Helsinki Heart Study, the incidence of total malignancies discovered during the trial and in the 1.5 years since the trial was completed was 39 in the Lipid group and 29 in the placebo group: p = 0.056. In the Helsinki Heart Study, the incidence of total malignancies discovered during the trial and in the 1.5 years since the trial was completed was 39 in the Lipid group and 29 in the placebo group: p = 0.056. In the Helsinki Heart Study, the incidence of total malignancies discovered during the trial and in the 1.5 years since the trial was completed was 39 in the Lipid group and 29 in the placebo group: p = 0.056. In the Helsinki Heart Study, the incidence of total malignancies discovered during the trial and in the 1.5 years since the trial was completed was 39 in the Lipid group and 29 in the placebo group: p = 0.056.

GI: RAISES HDL DRAMATICALLY REDUCES HEART ATTACK.

Adverse reactions reported by more than 1% of subjects include:

• GI: Diarrhea, dyspepsia, nausea, vomiting, abdominal pain, headache
• Skin: Rash, pruritus, urticaria

Lipid® (Gemfibrozil) 600-mg Tablets

Lipid® (Gemfibrozil Capsules and Tablets)

from controls in the incidence of liver tumors, but the doses tested were lower than those shown to be carcinogenic with other fibrate.

Male rats had a dose-related and statistically significant increase in biliary lipid-cystic tumors. The number of males at 10 times the human dose was 10 times the human dose.

Electron microscopy studies have demonstrated a florid hepatic peroxisome proliferation following Lipid administration to the male rat. An adequate study to test for peroxisome proliferation has not been done in human at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for humans at the dose tested for human...
Contraindications: PRINIVIL® (lisinopril, MS/D) is contraindicated in patients who are hypersensitive to this product and in patients with a history of angioedema related to previous treatment with an ACE inhibitor.

Warnings: Angioedema: Angioedema of the face, extremities, lips, tongue, glottis, and/or larynx has been reported in patients treated with ACE inhibitors, including PRINIVIL. In such patients, the incidence of angioedema is approximately 0.7% (see CLINICAL PHARMACOLOGY). Angioedema associated with laryngeal edema may be fatal. Where there is involvement of the tongue, glottis, or larynx, immediate intubation may be required. Where involvement is limited to the lips, tongue, or extremities, treatment with antihistamines and stay-in-bed status may suffice. In patients with angioedema, the use of ACE inhibitors is contraindicated (see DOSE AND ADMINISTRATION).

Hyperkalemia: In clinical trials, hyperkalemia (serum potassium >5.5 mEq/L) occurred in approximately 2.4% of hypertensive patients treated with PRINIVIL (see CLINICAL PHARMACOLOGY). In these patients, the incidence of serum potassium levels >6.5 mEq/L was approximately 0.1%. Some hypertensive patients with no apparent renal impairment and/or diuretic therapy may have been reported in patients treated with ACE inhibitors. The incidence of hyperkalemia in these patients should be evaluated, especially during the first few weeks of therapy. Serum potassium should be measured prior to initiation of therapy and at 3- to 7-week intervals thereafter. The use of potassium sparing diuretics, such as spironolactone, is not recommended in the initial treatment of hyperkalemia with PRINIVIL. If hyperkalemia occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Neutropenia/Agranulocytosis: Another ACE inhibitor has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment. Neutropenia and/or agranulocytosis have also been reported rarely in patients treated with PRINIVIL, who in some instances were on concomitant diuretics and/or corticosteroids. Some patients who develop neutropenia and/or agranulocytosis while receiving PRINIVIL are insufficient to show that PRINIVIL does not cause agranulocytosis at similar rates. Periodic differential white blood cell counts should be performed on patients receiving PRINIVIL, especially during the first few weeks of therapy. If granulocytopenia occurs, PRINIVIL should be promptly discontinued and the patient given without discontinuation of therapy, especially with a neutrophil count less than 1,000/mm3 or granulocytes less than 1000/mm3.

Neutropenia/Agranulocytosis: Another ACE inhibitor has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment. Neutropenia and/or agranulocytosis have also been reported rarely in patients treated with PRINIVIL, who in some instances were on concomitant diuretics and/or corticosteroids. Some patients who develop neutropenia and/or agranulocytosis while receiving PRINIVIL are insufficient to show that PRINIVIL does not cause agranulocytosis at similar rates. Periodic differential white blood cell counts should be performed on patients receiving PRINIVIL, especially during the first few weeks of therapy. If granulocytopenia occurs, PRINIVIL should be promptly discontinued and the patient given without discontinuation of therapy, especially with a neutrophil count less than 1,000/mm3 or granulocytes less than 1000/mm3.

Neutropenia/Agranulocytosis: Another ACE inhibitor has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment. Neutropenia and/or agranulocytosis have also been reported rarely in patients treated with PRINIVIL, who in some instances were on concomitant diuretics and/or corticosteroids. Some patients who develop neutropenia and/or agranulocytosis while receiving PRINIVIL are insufficient to show that PRINIVIL does not cause agranulocytosis at similar rates. Periodic differential white blood cell counts should be performed on patients receiving PRINIVIL, especially during the first few weeks of therapy. If granulocytopenia occurs, PRINIVIL should be promptly discontinued and the patient given without discontinuation of therapy, especially with a neutrophil count less than 1,000/mm3 or granulocytes less than 1000/mm3.

Neutropenia/Agranulocytosis: Another ACE inhibitor has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment. Neutropenia and/or agranulocytosis have also been reported rarely in patients treated with PRINIVIL, who in some instances were on concomitant diuretics and/or corticosteroids. Some patients who develop neutropenia and/or agranulocytosis while receiving PRINIVIL are insufficient to show that PRINIVIL does not cause agranulocytosis at similar rates. Periodic differential white blood cell counts should be performed on patients receiving PRINIVIL, especially during the first few weeks of therapy. If granulocytopenia occurs, PRINIVIL should be promptly discontinued and the patient given without discontinuation of therapy, especially with a neutrophil count less than 1,000/mm3 or granulocytes less than 1000/mm3.