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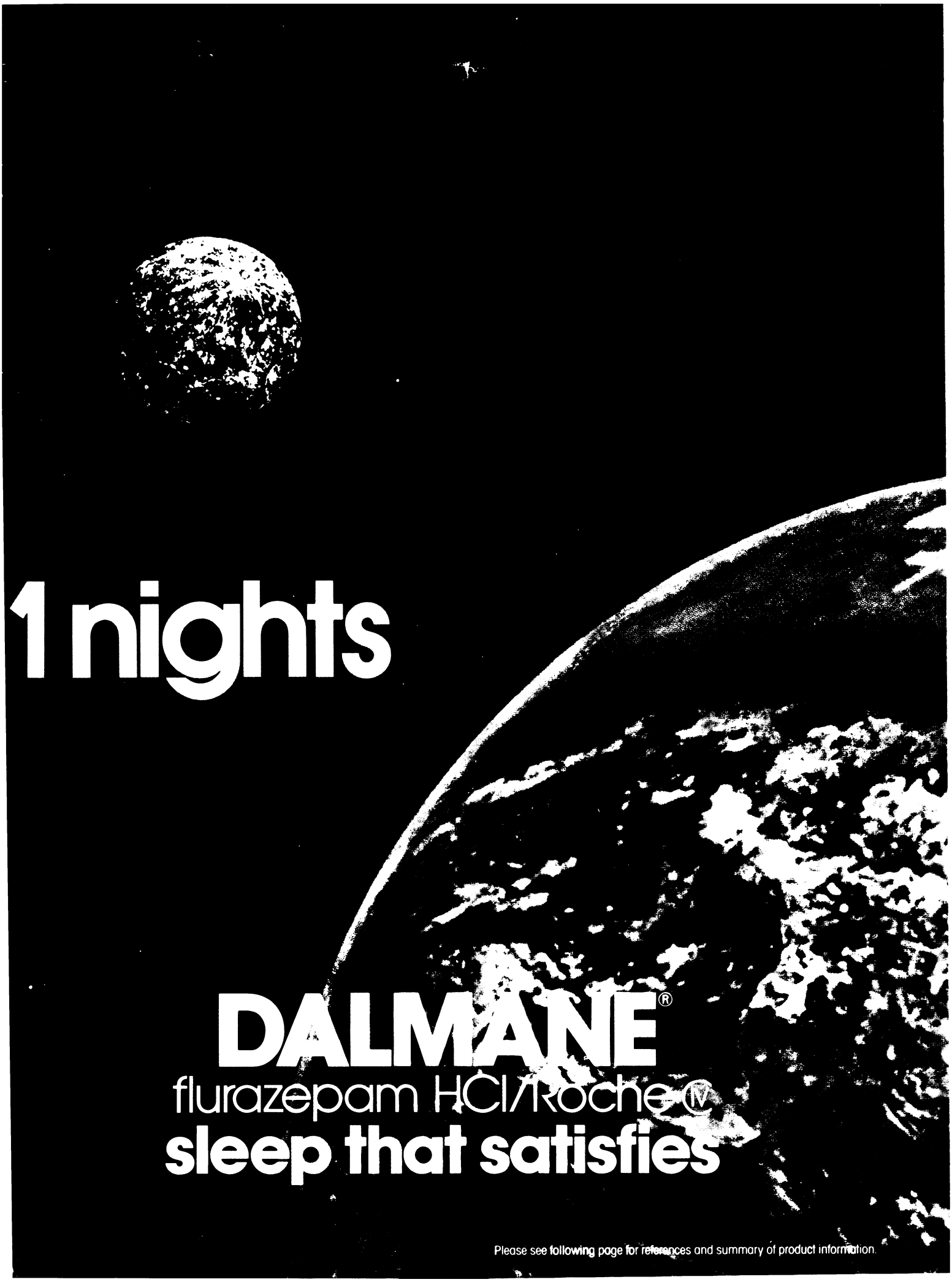
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Please see following page for references and summary of product information.

References: **1.** Kales J, *et al: Clin Pharmacol Ther 12*:691-697, Jul-Aug 1971. **2.** Kales A, *et al: Clin Pharmacol Ther 18*:356-363, Sep 1975. **3.** Kales A, *et al: Clin Pharmacol Ther 19*:576-583, May 1976. **4.** Kales A, *et al: Clin Pharmacol Ther 32*:781-788, Dec 1982. **5.** Frost JD Jr, DeLucchi MR: *J Am Geriatr Soc 27*:541-546, Dec 1979. **6.** Dement WC, *et al: Behav Med*, pp. 25-31, Oct 1978. **7.** Kales A, Kales JD: *J Clin Psychopharmacol 3*:140-150, Apr 1983. **8.** Tennant FS, *et al:* Symposium on the Treatment of Sleep Disorders, Teleconference, Oct 16, 1984. **9.** Greenblatt DJ, Allen MD, Shader RI: *Clin Pharmacol Ther 21*:355-361, Mar 1977.

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Contraindications: Known hypersensitivity to flurazepam HCl; pregnancy. Benzodiazepines may cause fetal damage when administered during pregnancy. Several studies suggest an increased risk of congenital malformations associated with benzodiazepine use during the first trimester. Warn patients of the potential risks to the fetus should the possibility of becoming pregnant exist while receiving flurazepam. Instruct patients to discontinue drug prior to becoming pregnant. Consider the possibility of pregnancy prior to instituting therapy.
Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nighttime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Withdrawal symptoms rarely reported; abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase dosage.
Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.
Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity.
Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg recommended initially until response is determined.
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In hypertension

CORGARD®

(nadolol tablets)

CORGARD® TABLETS
Nadolol Tablets

DESCRIPTION: Corgard (nadolol) is a synthetic nonselective beta-adrenergic receptor blocking agent.

CONTRAINDICATIONS: Bronchial asthma, sinus bradycardia and greater than first degree conduction block, cardiogenic shock, and overt cardiac failure (see WARNINGS).

WARNINGS: Cardiac Failure—Sympathetic stimulation may be a vital component supporting circulatory function in congestive heart failure, and its inhibition by beta-blockade may precipitate more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary, they can be used with caution in patients with a history of failure who are well-compensated, usually with digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle. IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta-blockers can, in some cases, lead to cardiac failure; therefore, at first sign or symptom of heart failure, digitalize and/or give diuretics, and closely observe response, or discontinue nadolol (gradually if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal—Hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after *abrupt* discontinuation of such therapy. When discontinuing chronic use of nadolol, particularly in patients with ischemic heart disease, gradually reduce dosage over a 1- to 2-week period and carefully monitor the patient. Reinstitute nadolol promptly (at least temporarily) and take other measures appropriate for management of unstable angina if angina markedly worsens or acute coronary insufficiency develops. Warn patients not to interrupt or discontinue therapy without physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue nadolol therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA-BLOCKERS. Administer nadolol with caution since it may block bronchodilation produced by endogenous or exogenous catecholamine stimulation of $beta_2$ receptors.

Major Surgery—Because beta-blockade impairs the ability of the heart to respond to reflex stimuli and may increase risks of general anesthesia and surgical procedures, resulting in protracted hypotension or low cardiac output, it has generally been suggested that such therapy should be withdrawn several days prior to surgery. Recognition of the increased sensitivity to catecholamines of patients recently withdrawn from beta-blocker therapy, however, has made this recommendation controversial. If possible, withdraw beta-blockers well before surgery takes place. In emergency surgery, inform the anesthesiologist that the patient is on beta-blocker therapy. Use of beta-receptor agonists such as isoproterenol, dopamine, dobutamine, or levarterenol can reverse the effects of nadolol. Difficulty in restarting and maintaining the heart beat has also been reported with beta-adrenergic receptor blocking agents.

Diabetes and Hypoglycemia—Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (e.g., tachycardia and blood pressure changes) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces release of insulin in response to hyperglycemia; therefore, it may be necessary to adjust dose of antidiabetic drugs.

Thyrotoxicosis—Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. To avoid abrupt withdrawal of beta-adrenergic blockade which might precipitate a thyroid storm, carefully manage patients suspected of developing thyrotoxicosis.

PRECAUTIONS: Impaired Renal Function—Use nadolol with caution (see DOSAGE AND ADMINISTRATION section of package insert).

Information for Patients—Warn patients, especially those with evidence of coronary artery insufficiency, against interruption or discontinuation of nadolol without physician's advice. Although cardiac failure rarely occurs in properly selected patients, advise patients being treated with beta-adrenergic blocking agents to consult physician at first sign of impending failure. Advise patients in event of missed doses.

Drug Interactions—Concurrent administration may result in interactions with: Anesthetics, general—exaggeration of the hypotension induced by general anesthetics (see WARNINGS, Major Surgery). Antidiabetic drugs (oral agents and insulin)—hypoglycemia or hyperglycemia; adjust antidiabetic drug dosage accordingly (see WARNINGS, Diabetes and Hypoglycemia). Catecholamine—depleting drugs (e.g., reserpine)—additive effect; monitor closely for hypotension and/or excessive bradycardia.

Carcinogenesis, Mutagenesis, Impairment of Fertility—In 1 to 2 years' oral toxicologic studies in mice, rats, and dogs, nadolol did not produce significant toxic effects. In 2-year oral carcinogenic studies in rats and mice, nadolol did not produce neoplastic, preneoplastic, or nonneoplastic pathologic lesions.

Pregnancy—In animal reproduction studies with nadolol, evidence of embryo-and fetotoxicity was found in rabbits (but not in rats or hamsters) at doses 5 to 10 times greater (on a mg/kg basis) than maximum indicated human dose; no teratogenic potential was seen in any of these species. There are no well-controlled studies in pregnant women; therefore, use nadolol in pregnant women only if potential benefit justifies potential risk to the fetus. Neonates of mothers who received nadolol at parturition have exhibited bradycardia, hypoglycemia and associated symptoms.

Nursing Mothers—Nadolol is excreted in human milk. Exercise caution when nadolol is administered to a nursing woman.

Pediatric Use—Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Most adverse effects have been mild and transient and have rarely required nadolol withdrawal.

Cardiovascular—Bradycardia with heart rates of less than 60 beats per minute occurs commonly, and heart rates below 40 beats per minute and/or symptomatic bradycardia were seen in about 2 of 100 patients. Symptoms of peripheral vascular insufficiency, usually of the Raynaud type, have occurred in approximately 2 of 100 patients. Cardiac failure, hypotension, and rhythm/conduction disturbances have each occurred in about 1 of 100 patients. Single instances of first degree and third degree heart block have been reported; intensification of AV block is a known effect of beta-blockers (see also CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS). **Central Nervous System**—Dizziness or fatigue reported in approximately 2 of 100 patients; paresthesias, sedation, and change in behavior reported in approximately 6 of 1000 patients. **Respiratory**—Bronchospasm reported in approximately 1 of 1000 patients (see CONTRAINDICATIONS and WARNINGS). **Gastrointestinal**—Nausea, diarrhea, abdominal discomfort, constipation, vomiting, indigestion, anorexia, bloating and flatulence each reported in 1 to 5 of 1000 patients. **Miscellaneous**—Each of the following reported in 1 to 5 of 1000 patients: rash; pruritus; headache; dry mouth, eyes, or skin; impotence or decreased libido; facial swelling; weight gain; slurred speech; cough; nasal stuffiness; sweating; tinnitus; blurred vision; infrequent reversible alopecia. The following adverse reactions have been reported in patients taking nadolol and/or other beta-adrenergic blocking agents, but no causal relationship to nadolol has been established. **Central Nervous System**—reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place; short-term memory loss, emotional lability with slightly clouded sensorium; decreased performance on neuropsychometrics. **Gastrointestinal**—mesenteric arterial thrombosis; ischemic colitis; elevated liver enzymes. **Hematologic**—agranulocytosis; thrombocytopenic or nonthrombocytopenic purpura. **Allergic**—fever combined with aching and sore throat; laryngospasm; respiratory distress. **Miscellaneous**—pemphigoid rash; hypertensive reaction in patients with pheochromocytoma; sleep disturbances; Peyronie's disease. The oculomucocutaneous syndrome associated with practolol has not been reported with nadolol.

OVERDOSAGE: Nadolol can be removed from the general circulation by hemodialysis. In addition to gastric lavage, employ the following measures as appropriate. In determining duration of corrective therapy, take note of long duration of effect of nadolol.

Excessive Bradycardia—Administer atropine (0.25 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.

Cardiac Failure—Administer a digitalis glycoside and diuretic. It has been reported that glucagon may also be useful in this situation.

Hypotension—Administer vasopressors, e.g., epinephrine or levarterenol. (There is evidence that epinephrine may be the drug of choice.)

Bronchospasm—Administer a $beta_2$-stimulating agent and/or a theophylline derivative.

DOSAGE: For all patients, DOSAGE MUST BE INDIVIDUALIZED.

For **angina pectoris,** usual initial dose is 40 mg q.d.; may be gradually increased in 40 to 80 mg increments at 3 to 7 day intervals until optimum clinical response or pronounced slowing of the heart rate; usual maintenance dose is 40 or 80 mg q.d. (doses up to 160 or 240 mg daily may be needed). If treatment is to be discontinued, reduce dosage gradually over a period of 1 to 2 weeks (see WARNINGS).

For **hypertension,** usual initial dose is 40 mg q.d.; gradually increase in 40 to 80 mg increments until optimum blood pressure reduction is achieved; usual maintenance dose is 40 or 80 mg q.d. (doses up to 240 or 320 mg daily may be needed).

Patients with renal failure require adjustment in dosing interval; see package insert for dosage in these patients.

For full prescribing information, consult package insert.

HOW SUPPLIED: In scored tablets containing 40, 80, 120, or 160 mg nadolol per tablet in bottles of 100 and in Unimatic® unit-dose packs of 100 tablets. The 40 mg, 80 mg, and 120 mg potencies are also available in bottles of 1000 tablets. (J3-527D)

References: 1. Epstein M, Oster JR: Beta-blockers and the kidney. Min Electrolyte Metab 8:237-254, 1982. 2. Danesh BJZ, et al: Comparison between short-term renal haemodynamic effects of propranolol and nadolol in essential hypertension: a cross-over study. Clin Sci 67:243-248, 1984. 3. Hollenberg NK: Introduction: β-adrenergic blocking agents–the treatment of hypertension and the kidney. Royal Soc of Med Int Congress and Symposium Series 51:1-8, 1982. 4. Frohlich ED, et al: Long-term renal hemodynamic effects of nadolol in patients with essential hypertension. Am Heart J 108:1141-1143, 1984. 5. Alexander JC, et al: Long-term experience with nadolol in treatment of hypertension and angina pectoris. Am Heart J 108:1136-1140, 1984.

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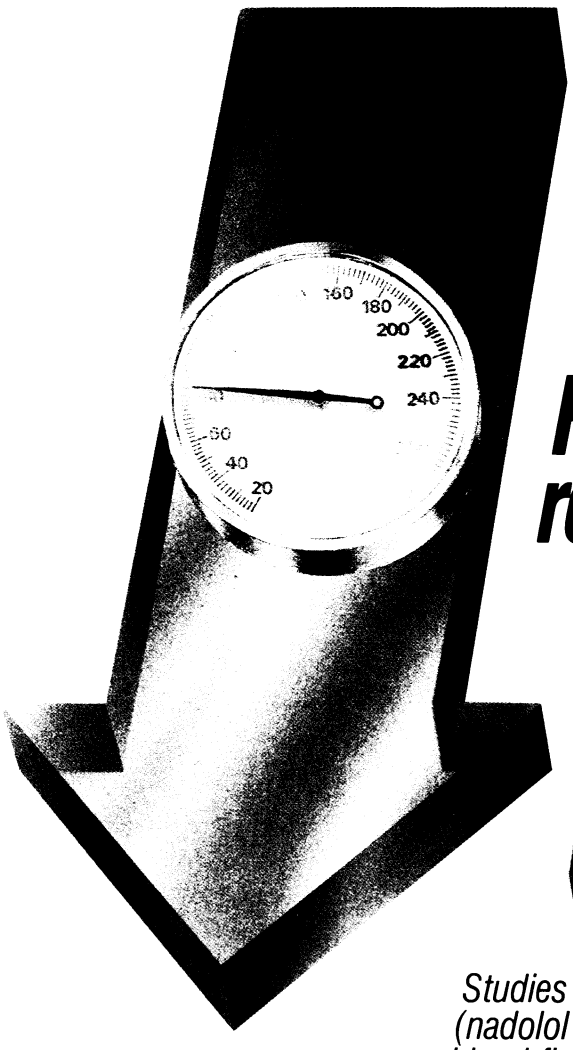

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Description: THEO-DUR sustained action tablets contain anhydrous theophylline, a bronchodilator, in a sustained release formulation (with no color additives) which allows a 12-hour dosing interval for a majority of patients and a 24-hour dosing interval for selected patients.
Clinical Pharmacology: Theophylline directly relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, thus acting mainly as a bronchodilator and smooth muscle relaxant. The drug also produces other actions typical of the xanthine derivatives: coronary vasodilator, cardiac stimulant, diuretic, cerebral stimulant, and skeletal muscle stimulant. The actions of theophylline may be mediated through inhibition of phosphodiesterase and a resultant increase in intracellular cyclic AMP. Apparently, no development of tolerance occurs with chronic use of theophylline.
Indications: THEO-DUR is indicated for relief and/or prevention of symptoms of bronchial asthma and for reversible bronchospasm associated with chronic bronchitis and emphysema.
Contraindications: THEO-DUR is contraindicated in individuals who have shown hypersensitivity to theophylline or any of the tablet components.
Warnings: Excessive theophylline doses may be associated with toxicity; serum theophylline levels should be monitored to insure maximum benefit with minimum risk. Incidence of toxicity increases at serum levels greater than 20 mcg/ml. High blood levels of theophylline resulting from conventional doses are correlated with clinical manifestation of toxicity in: patients with lowered body plasma clearances, patients with liver dysfunction or chronic obstructive lung disease, and patients who are older than 55 years of age, particularly males. There are often no early signs of less serious theophylline toxicity such as nausea and restlessness, which may occur in up to 50% of patients prior to onset of convulsions. Ventricular arrhythmias or seizures may be the first signs of toxicity. Many patients who have higher theophylline levels exhibit tachycardia. Theophylline products may worsen pre-existing arrhythmias.
Precautions: THEO-DUR TABLETS SHOULD NOT BE CHEWED OR CRUSHED. Theophylline should not be administered concurrently with other xanthine medications. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, liver disease, in the elderly (especially males) and in neonates. In particular, great caution should be used in giving theophylline to patients with congestive heart failure. Frequently, such patients have markedly prolonged theophylline serum levels with theophylline persisting in serum for long periods following discontinuation of the drug. Use theophylline cautiously in patients with history of peptic ulcer. Theophylline may occasionally act as a local irritant to the G.I. tract although gastrointestinal symptoms are more commonly centrally mediated and associated with serum drug concentrations over 20 mcg/ml.
Individuals who are rapid metabolizers of theophylline, such as the young, smokers, and some non-smoking adults, may not be suitable candidates for once-daily dosing. These individuals will generally need to be dosed at 12 hourly or sometimes 8 hourly intervals. Such patients may exhibit symptoms of bronchospasm near the end of a dosing interval, or may have wider peak-to-trough differences than desired.
Usage in Pregnancy: Animal reproduction studies have not been conducted with theophylline. It is not known whether theophylline can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Xanthines should be given to a pregnant woman only if clearly needed.
Nursing Mothers: It has been reported that theophylline distributes readily into breast milk and may cause adverse effects in the infant. Caution must be used if prescribing xanthines to a mother who is nursing, taking into account the risk-benefit of this therapy.
Pediatric Use: Safety and effectiveness of THEO-DUR administered every 24 hours in children under 12 years of age, and every 12 hours in children under 6 years of age, have not been established.
Adverse Reactions: The most consistent adverse reactions are usually due to overdose and are:
Gastrointestinal: nausea, vomiting, epigastric pain, hematemesis, diarrhea.
Central nervous system: headaches, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.
Cardiovascular: palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, ventricular arrhythmias.
Respiratory: tachypnea.
Renal: albuminuria, increased excretion of renal tubular and red blood cells, potentiation of diuresis.
Others: rash, hyperglycemia and inappropriate ADH syndrome.
How Supplied: THEO-DUR 100 mg, 200 mg and 300 mg sustained action tablets are available in bottles of 100, 500, 1000 and 5000, and in unit dose packages of 100.
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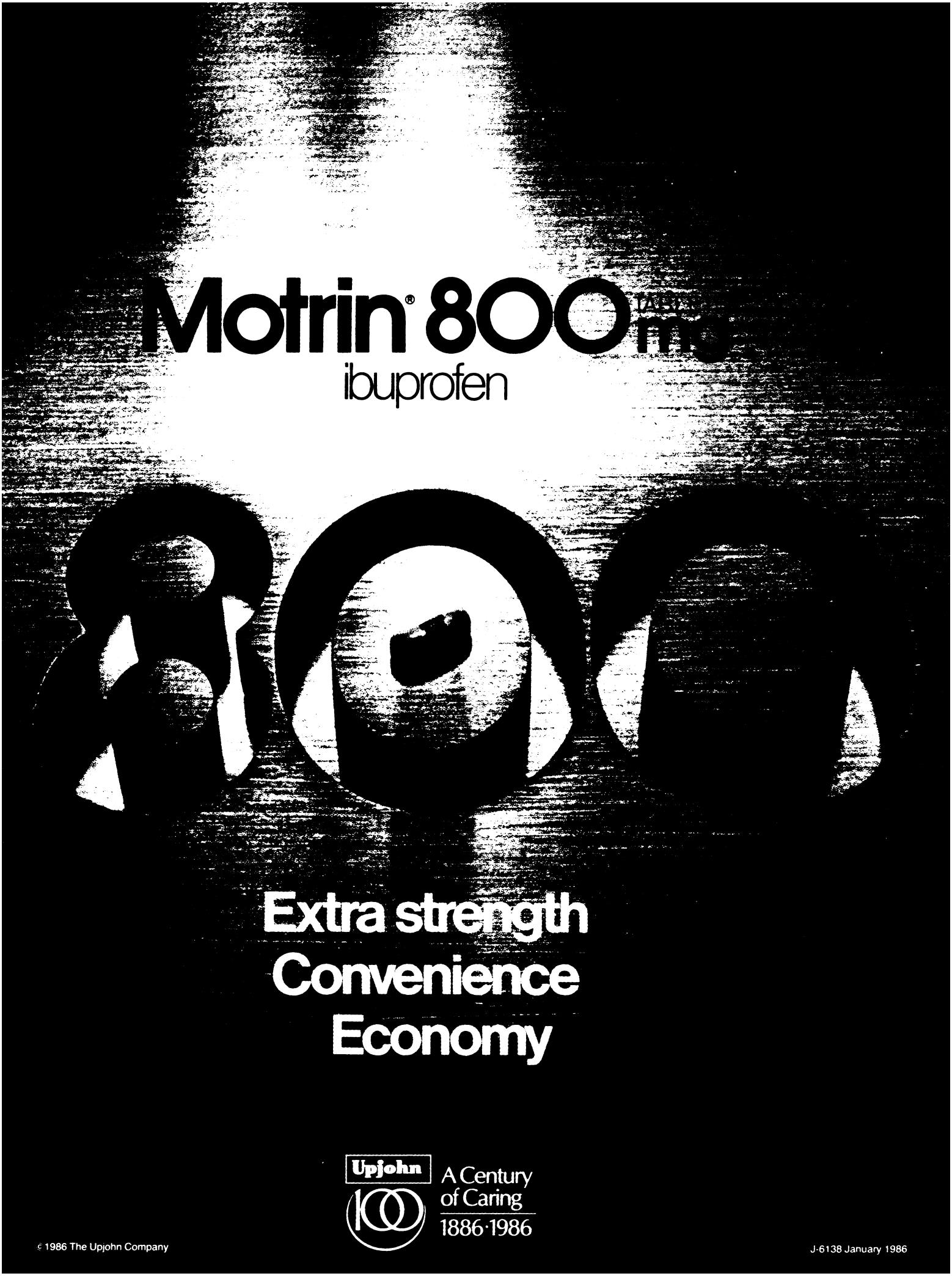

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*angiotensin-converting enzyme

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IN MILD TO MODERATE HYPERTENSION

IT MAY CHANGE THE WAY YOUR PATIENTS FEEL ON ANTIHYPERTENSIVE THERAPY

VASOTEC® (Enalapril Maleate, MSD) is contraindicated in patients who are hypersensitive to this product.

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In Worldwide Controlled Clinical Trials

Generally Well Tolerated— Overall Percentage of Patients Reporting Adverse Effects Comparable to Placebo

Incidence of Most Frequent Adverse Effects as Compared with Placebo in Controlled Clinical Trials

	VASOTEC* n = 2,677	Placebo n = 230
HEADACHE	4.8%	9.1%
DIZZINESS	4.6	4.3
FATIGUE	2.8	2.6
DIARRHEA	1.6	1.7
RASH	1.5	0.4
HYPOTENSION	1.4	0.4
NAUSEA	1.3	1.7
COUGH	1.3	0.9
ORTHOSTATIC EFFECTS	1.3	0.0

*Includes 363 patients treated for congestive heart failure receiving concomitant digoxin and diuretic therapy. Data include adverse effects for VASOTEC with an incidence greater than 1%.

- For the most part, adverse effects were mild and transient and usually did not require discontinuation of therapy.
- In clinical trials, the overall frequency of adverse effects was not related to total daily dosage within the range of 10 to 40 mg.
- Incidence of impotence was only 0.7%.

Angioedema has been reported in patients treated with angiotensin-converting-enzyme inhibitors, including VASOTEC (0.2% of patients treated with VASOTEC). Angioedema associated with laryngeal edema and/or shock may be fatal. **If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately** (see ADVERSE REACTIONS).

FOR MANY HYPERTENSIVE PATIENTS

ONCE-A-DAY

NEW VASOTEC®

(ENALAPRIL MALEATE | MSD)

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

NEW VASOTEC

(ENALAPRIL MALEATE | MSD)

Contraindications: VASOTEC® (Enalapril Maleate, MSD) is contraindicated in patients who are hypersensitive to this product.

Warnings: *Angioedema:* Angioedema has been reported in patients treated with angiotensin-converting-enzyme inhibitors, including VASOTEC. Angioedema associated with laryngeal edema and/or shock may be fatal. **If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately.** (See ADVERSE REACTIONS.)

Hypotension: Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of enalapril use in severely salt/volume-depleted persons such as those treated vigorously with diuretics or patients on dialysis. (See PRECAUTIONS, *Drug Interactions* and ADVERSE REACTIONS.) In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased.

If hypotension occurs, the patient should be placed in supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which usually can be given without difficulty once the blood pressure has increased after volume expansion.

Neutropenia/Agranulocytosis: Another angiotensin-converting-enzyme inhibitor has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: *General: Impaired Renal Function:* In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients renal function should be monitored during the first few weeks of therapy.

Some hypertensive patients with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction of VASOTEC and/or discontinuation of the diuretic may be required.

Hyperkalemia: Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. Risk factors for the development of hyperkalemia may include renal insufficiency, diabetes mellitus, and the concomitant use of agents to treat hypokalemia. (See *Drug Interactions*.)

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients:

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, eyes, lips, tongue, difficulty in breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions:

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. (See WARNINGS and DOSAGE AND ADMINISTRATION.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC® (Enalapril Maleate, MSD) is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: VASOTEC has been used concomitantly with beta adrenergic-blocking agents, methyldopa, nitrates, calcium-blocking agents, hydralazine, and prazosin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: VASOTEC may attenuate potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated, they should be used with caution and with frequent monitoring of serum potassium.

Pregnancy—Category C: There was no fetotoxicity or teratogenicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity, expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril, but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

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

Nursing Mothers: It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

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

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2677 patients.

The most frequent clinical adverse experiences in controlled trials were: headache (4.8%), dizziness (4.6%), and fatigue (2.8%). For the most part, adverse experiences were mild and transient in nature. Discontinuation of therapy was required in 6.0% of patients. In clinical trials, the overall frequency of adverse experiences was not related to total daily dosage within the range of 10 to 40 mg. The overall percentage of patients treated with VASOTEC reporting adverse experiences was comparable to placebo.

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were: diarrhea (1.6%), rash (1.5%), hypotension (1.4%), cough (1.3%), nausea (1.3%), and orthostatic effects (1.3%).

Clinical adverse experiences occurring in 0.5% to 1.0% of patients in the controlled trials included:

Cardiovascular: Syncope, orthostatic hypotension, palpitations, chest pain.

Nervous System: Insomnia, nervousness, paresthesia, somnolence.

Gastrointestinal System: Abdominal pain, vomiting, dyspepsia.

Other: Dyspnea, muscle cramps, hyperhydrosis, impotence, pruritus, asthenia.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema and/or shock may be fatal. If angioedema of the face, tongue, or glottis occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: Combining the results of clinical trials in patients with hypertension or congestive heart failure, hypotension (including postural hypotension and other orthostatic effects) was reported in 2.3% of patients following the initial dose of enalapril or during extended therapy. In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 0.1% of hypertensive patients. (See WARNINGS.)

Clinical Laboratory Test Findings:

Hyperkalemia: (See PRECAUTIONS.)

Creatinine, Blood Urea Nitrogen: Minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.)

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol%, respectively) occur frequently in hypertensive patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): Rarely, elevations of liver enzymes and/or serum bilirubin have occurred.

In overseas marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported.

For more detailed information, consult your MSD representative or see Prescribing Information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19486.

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MSD
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Developing primary and permanent teeth supplied with systemic fluoride are so much stronger that caries can be reduced 50-80% during childhood.[1,2]

Since pre-eruptive teeth incorporate fluoride more easily than erupted teeth,[3] systemic fluoride is recommended every day from birth.

Breast milk and Ready-To-Use (RTU) formulas contain only trace amounts of fluoride.

So, even if a nursing mother drinks fluoridated water, a fluoride supplement for baby is needed when breast milk or RTU formulas are baby's main food sources.

Provide the fluoride infants need.

Prescribe Vi-Flor® vitamin-fluoride supplements soon after birth.

See accompanying full prescribing information.

REFERENCES:
[1]Aasenden R and Peebles T: Effects of fluoride supplementation from birth on human deciduous and permanent teeth. Arch Oral Biol 1974; 19:321.
[2]Hambert L: Controlled trial of fluoride in vitamin drops for prevention of caries in children. Lancet 1971 Feb. 27; p 442.
[3]Newbrun E: How Fluoride Works: Topical vs. Systemic Action, in Mead Johnson Clinical Report Series, Clinical Importance of Fluoride Nutrition in Infants, Children and Young Adults, Chicago, Pragmaton®, 1985, p 7.

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NUTRITIONAL DIVISION

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PHYSICIANS ADDRESS THE ISSUES AT THE UTAH STATE MEDICAL ASSOCIATION ANNUAL MEETING

September 10, 11, 12, 1986
The Yarrow
Park City, Utah

Schedule of Events

Wednesday, September 10

9:00 AM	**Hospital Medical Staff Section**
9:30 AM	**USMA House of Delegates Opening Session**
12:00 NOON	**Luncheon** *Speaker: John J. Coury, Jr., M.D.* *President-Elect* *American Medical Association*
1:30 PM	**Reference Committee Meetings**
4:00 PM	**USMA House of Delegates**
7:30 PM	**Barbeque**

Thursday, September 1

7:00 PM — **Fun Run - 3k and 10k Races**

9:00 AM — **Converging Pressures: A Changing Profession**
Forum on Medical Issues

Entrepreneurialism and Professionalism: When Do They Conflict?
George D. Lundberg, M.D., Editor,
Journal of American Medical Association

A Federal Solution to the Malpractice Crisis
David N. Sundwall, M.D., Staff Assistant
Labor & Human Resources Committee, U.S. Senate

Making Decisions Washington Style: The Doctor's Dilemma
John C. Nelson, M.D., Commissioner
Federal Prospective Payment Assessment Commission

Physician Alternatives in Health Care Delivery
Allan H. Goodman, M.D., Chairman of the Board
Western Health Plans, Inc.,
San Diego California.

12 Noon — **Luncheon Speaker: Ambassador David Kennedy**

Afternoon — **Golf - Tennis**

6:30 PM — **Presidents' Dinner**

Friday, September 12

9:00 AM — **Medical Problems with Social Consequences**

Aids
Paul A. Volberding, M.D.
Chief, AIDS Activities Division
San Francisco General Hospital

Alzheimers
Murray Raskin, M.D.
Director for Geriatric Research, Education And Clinical Center
Seattle & American Lake VA Hospitals
(Speaker sponsored by Roerig-Pfizer Company)

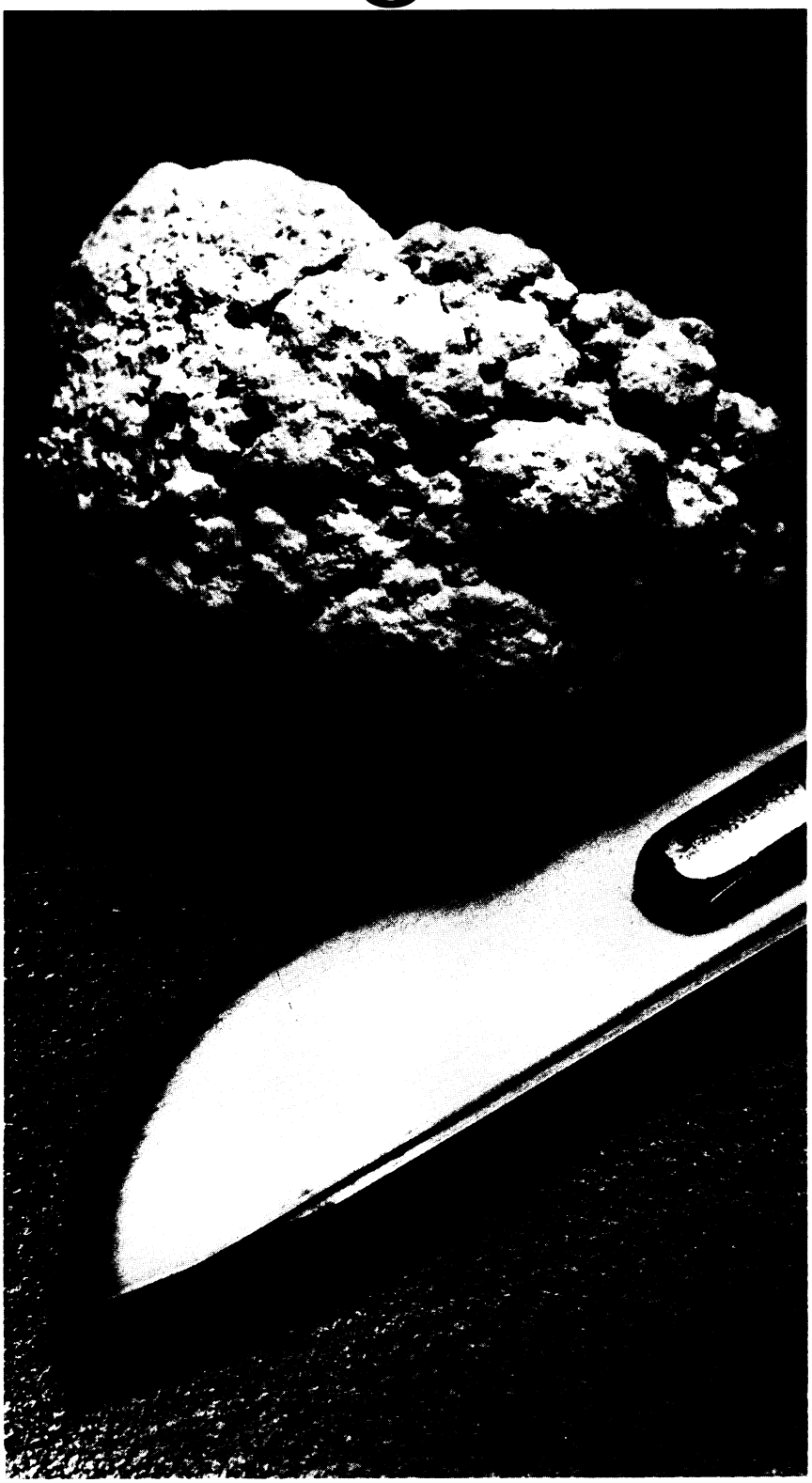
Abuse of Children
Frederic N. Silverman, M.D.
Clinical Professor of Radiology
University of California, San Francisco

12:00 Noon — **Luncheon Meeting**

Medical Liability Loss Prevention
Special training for Prevention Coordinators & practical information for doctors who wish to minimize risk of malpractice in their hospitals and offices.
John B. Stanchfield, M.D.
Medical Director
Utah Medical Insurance Association

Reservation forms available from:
USMA, 540 East Fifth South, Salt Lake City, UT 84102 • (801) 355-7477

We're bringing urologists out of the Stone Age.



Now you can give your patients an inexpensive, timesaving alternative to invasive kidney stone surgery: Extra Corporeal Shock Wave Lithotripsy at the Western Kidney Stone Center.

Our open staff privileges allow trained, qualified urologists quick and easy access to an FDA approved Dornier lithotripter. Revolutionary, non-invasive technology that can not only crumble a kidney stone, but also split the cost of conventional surgery in half for your patient. It also has the ability to change weeks of recovery into days.

If you haven't yet received lithotripsy training, our program can assist you in getting the specialized education needed to perform the procedure. In the meantime, we can refer you to a trained urologist who will work with you, not in place of you. One who will supply you with a complete description of your patients' case, operative notes, and specific follow-up care needs. All patients are sent back to the referring physician for follow-up care.

Bottom Line: The Western Kidney Stone Center gives urologists the ability to recommend lithotripsy, without recommending another doctor. It's a service that will not only help you keep your patients, but one that will also keep you in the forefront of your profession.

Call our Clinical Coordinator for more information on the procedure, eligibility criteria, and scheduling dates.

If you're out-of-state, dial: 1-800-84STONE.

If you're in-state: 1-800-64STONE.

Western Kidney Stone Center

At Community Hospital of Los Gatos
815 Pollard Road
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A NATIONAL MEDICAL ENTERPRISES FACILITY

Give your angina patient added protection...

CARDIZEM®: FEWER SIDE EFFECTS

diltiazem HCl/Marion

- ***The lowest incidence of side effects among the calcium channel blockers***[1]
- ***An exceptionally safe choice for angina patients with coexisting hypertension, diabetes, asthma, or COPD***[1-3]
- ***Proven efficacy when used alone in angina***[1,4-6]
- ***Compatible with both beta-blockers and nitrates***[7]

Please see brief summary of prescribing information on the next page.

CARDIZEM® 60 mg tid or qid

diltiazem HCl/Marion

FEWER SIDE EFFECTS IN ANTIANGINAL THERAPY

BRIEF SUMMARY

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist).

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

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, and (3) patients with hypotension (less than 90 mm Hg systolic).

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 (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
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 (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored 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 which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left [illegible] In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. 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 some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM (diltiazem hydrochloride) in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

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.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme, leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy** — CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

CARDIZEM 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other. Issued 4/1/84

See complete Professional Use Information before prescribing.

0642T5

References: 1. *Physicians' Desk Reference®*, ed 39. Oradell, NJ: Medical Economics Company Inc, 1985. 2. Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): *Heart Disease: A Textbook of Cardiovascular Medicine*, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39. 3. Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. *Mod Med* 1982; 50(Sept):94-116. 4. Subramanian VB: Comparative evaluation of four calcium antagonists and propranolol with placebo in patients with chronic stable angina. *Cardiovasc Rev Rep* 1984; 5:91-104. 5. Schroeder JS, Feldman RL, Giles TD, et al: Multiclinic controlled trial of diltiazem for Prinzmetal's angina. *Am J Med* 1982; 72:227-231. 6. Weiner DA, McCabe CH, Cutler SS, et al: The efficacy and safety of high-dose verapamil and diltiazem in the long-term treatment of stable exertional angina. *Clin Cardiol* 1985; 7:648-653. 7. Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. *Consultant* 1984; 24(Dec):150-159.

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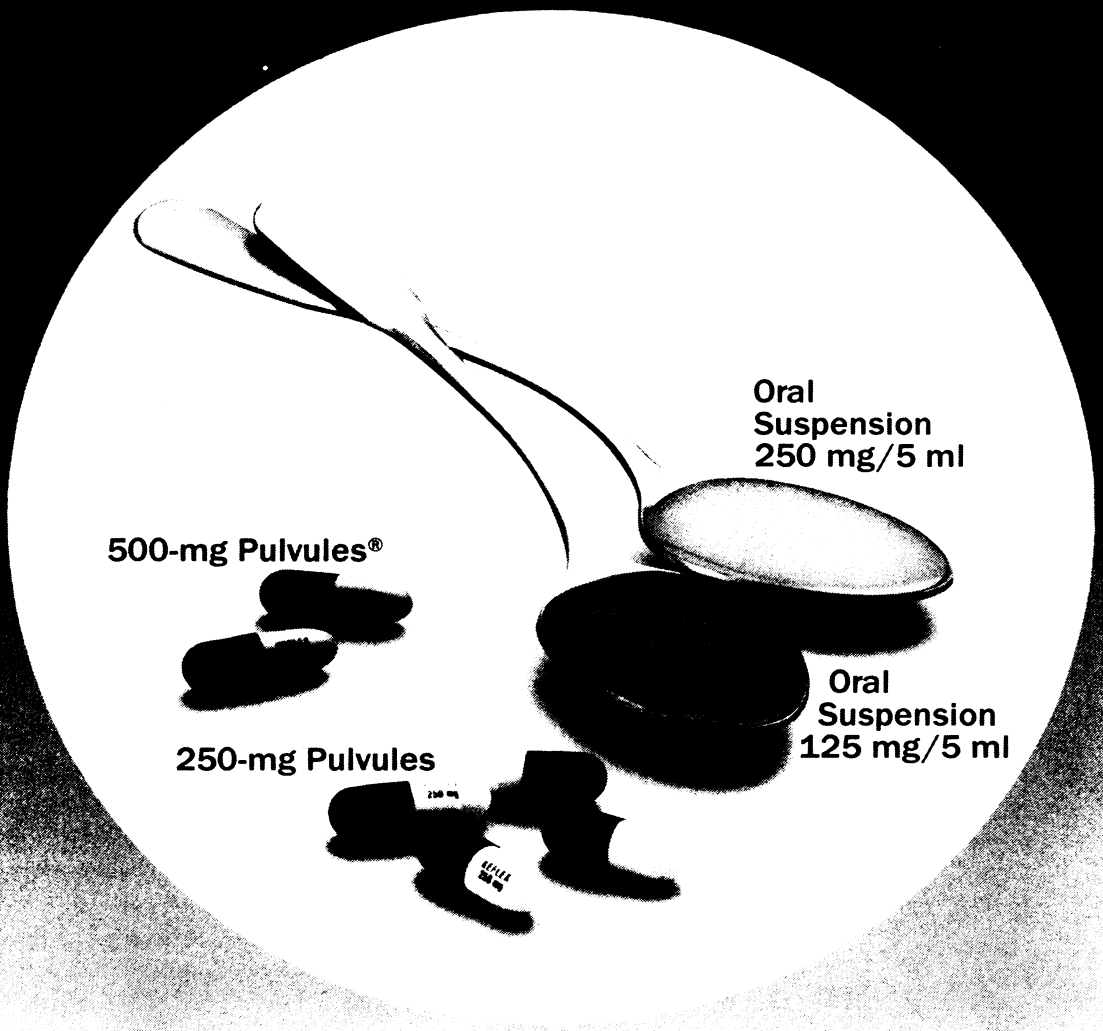

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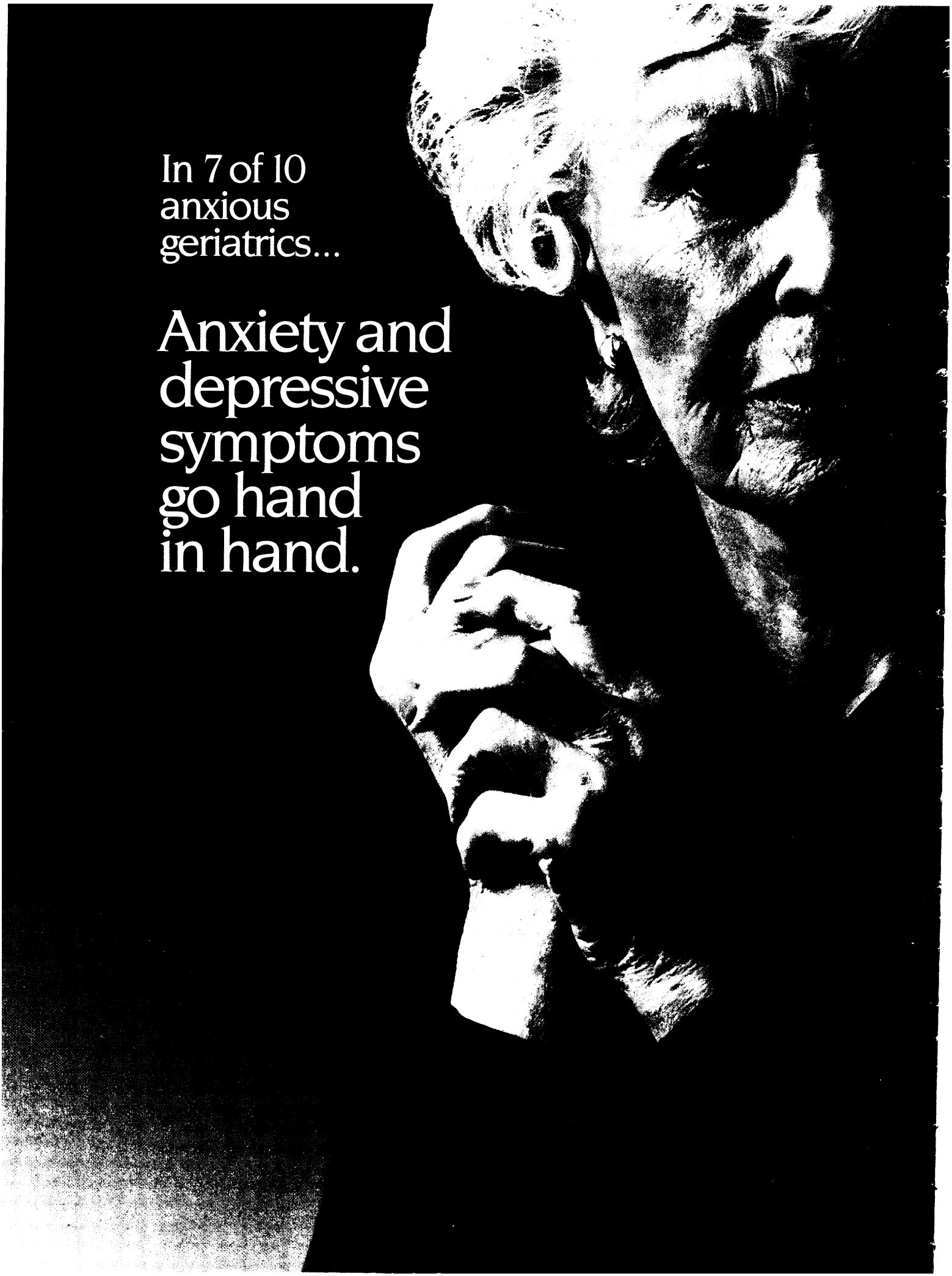
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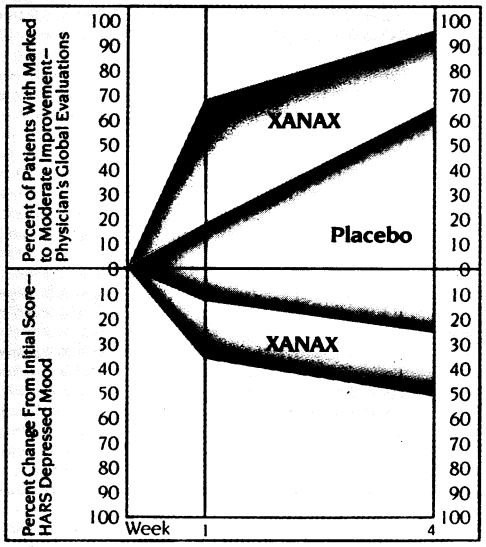
in hand.

Xanax effectively relieves anxiety with associated depressive symptoms.



In a recent clinical study[1] of 83 geriatric patients with clinical anxiety, 73% were diagnosed as having symptoms of depressed mood.

XANAX is well suited for therapy because it demonstrates greater efficacy than does placebo in reducing the Hamilton Anxiety Rating Scale Total Score and individual items, including depressed mood (see Figure).

With clinical advantages for geriatric patients.

- Effectively relieves the symptoms of anxiety
- Also relieves anxiety with associated depressed mood
- Well tolerated—side effects, if they occur, are generally observed at the beginning of therapy and usually disappear with continued medication. Drowsiness and light-headedness were the most commonly reported adverse reactions
- Does not cause cardiovascular toxicity
- **Specific geriatric dosage**—0.25 mg, two or three times daily

1. Cohn JB: Double-blind safety and efficacy comparison of alprazolam and placebo in the treatment of anxiety in geriatric patients. *Curr Ther Res* 1984;35(1):100-112.

Xanax® 0.25 mg Tablets
alprazolam IV

Upjohn 100 A Century of Caring 1886·1986

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Kalamazoo, Michigan 49001, USA

Please see adjacent page for brief summary of prescribing information.

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**
This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both; hyperglycemia and glycosuria (diabetic insulin requirements may be altered); hyperuricemia and gout; digitalis intoxication (in hypokalemia); decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS:DZ:L42

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Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).

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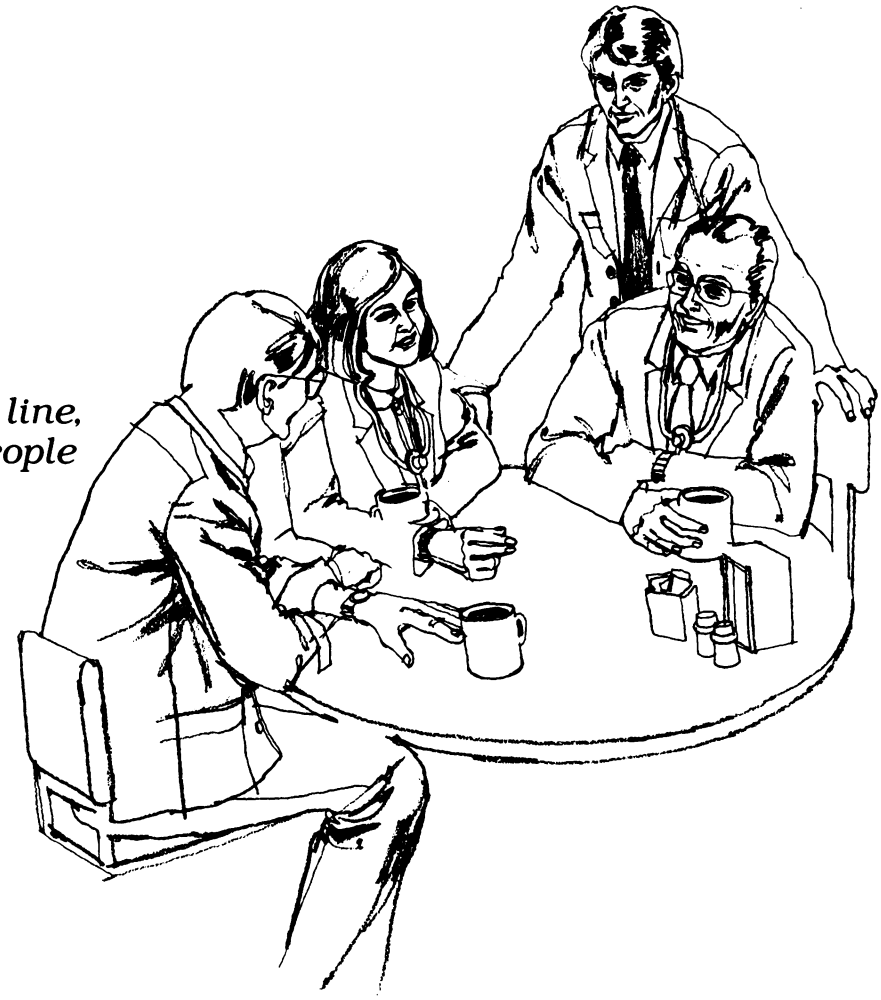

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MONTEREY PENINSULA, California Board certified/eligible general Internist to join five other Internists now in multispecialty group. Guaranteed income arrangement leading to partnership. Busy, well established clinic practice. Excellent office, lab, x-ray equipment. Outstanding community hospital. Submit CV, availability date to John D. Lord, MD, Central Medical Group, Monterey Peninsula, Pacific Grove, CA 93950.

INTERNIST with sub-speciality to join six established in Mountain View, California. Near 450 bed, well equipped hospital and Stanford University. Send CV to El Camino Internal Medical Group, Inc., 125 South Dr., Mountain View, CA 94040.

NEPHROLOGIST WANTED. Join group Nephrologists in Central California. Acute and chronic hemodialysis facilities available. Salary negotiable. Reply to Number 122, The Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

SAN BRUNO, CALIFORNIA—Full service medical building near two major hospitals and San Francisco airport. Wanted—Ophthalmologist, Dermatologist and Pediatrician. Call S. Glafkides, 1001 Sneath Lane, Suite 300, San Bruno, CA 94066; (415) 583-5515.

FAMILY OR GENERAL PRACTICE PHYSICIAN needed for an innovative primary health care system. Excellent salary, fringe benefits and continuing educational opportunities. Write to PO Box 3239, Farmington, NM 87499.

FAMILY PRACTICE opportunity in Tucumcari, New Mexico. Join physician in a lucrative established practice. Guaranteed income for the right individual. Family-oriented community with a wide range of recreational opportunities—great weather in the Sunbelt. Submit CV to: Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666; or call 1 (800) 545-4030, ext. 8300.

PHYSICIANS WANTED

SAN FRANCISCO—Full- and part-time positions available immediately for physicians Board certified/eligible in Emergency Medicine, Internal Medicine or Family Practice. Ambulatory Care service in Chinatown area of San Francisco. Guaranteed hourly, paid malpractice, 24-hour shifts. Prefer Chinese-speaking. Submit CV to Chase Dennis Group, 873 Corcoran Ct., Benicia, CA 94510.

SAN FRANCISCO BAY AREA—Director, Department of Anesthesia. Community Hospital, a 145-bed acute care teaching facility owned by Sonoma County and managed by National Medical Enterprises, Inc., is seeking a BC/BE Anesthesiologist with extensive clinical experience and demonstrated management ability. Located 60 miles north of San Francisco in the heart of the wine country, the hospital is affiliated with the UC School of Medicine and offers a nationally recognized three year Family Practice Medicine Residency Program as well as a full range of services from a Level-2 ICN to Outpatient Clinics. Send CV by 8/1/86 to: Search Committee, c/o Office of the Administrator, Community Hospital, 3325 Chanate Rd., Santa Rosa, CA 95404. EOE/AA.

GENERAL INTERNIST: Excellent professional opportunity. Internal Medicine associate to join solo practitioner in rapidly expanding rural area of Northern San Diego County. Less than one hour drive from San Diego. Send CV, ASAP to S. Michael Roche, MD, 591 E. Elder, Ste. C, Fallbrook CA 92028; (619) 723-1101.

PART-TIME POSITIONS available for qualified, experienced physicians in busy suburban Emergency Department. Excellent access to consultative services. San Francisco Bay area. Contact T. Del Presto, MD, Chief, Emergency Department, Kaiser Foundation Hospital, 1150 Veterans Blvd., Redwood City, CA 94063 or call (415) 780-2208.

ONCOLOGIST/HEMATOLOGIST, BC/BE—Immediate opening to replace a retiring Oncologist in a 32-physician, multispecialty group located in the Pacific Northwest. Radiation therapy available in community. Guaranteed salary and immediate full participation in incentive program, plus outstanding benefit package. Please submit your CV to the Search Committee, Walla Walla Clinic, 55 West Tietan, Walla Walla, WA 99362.

FAMILY PRACTITIONER/INTERNIST BE/BC sought for a busy solo General Practitioner in a growing Northern California community 40 miles from San Francisco Bay. No OB. Flexible hours. Send CV to: Megan Thurmond, MD, 108 Lynch Creek Way, #4, Petaluma, CA 94952.

PHYSICIANS WANTED

PACIFIC NORTHWEST OPPORTUNITIES FOR OB/GYNS

(1) Urban women's group private practice with hospital support; (2) full spectrum of OB/GYN including high risk for a busy, urban multispecialty clinic; (3) GYN or OB/GYN private practice in SW Washington community with first-year guarantee. To find out how these settings can meet your personal and professional goals, send curriculum vitae or call: The Friedrich Group, Inc., 9284 Ferncliff Northeast, Bainbridge Island, WA 98110; (206) 842-5248 or 527-3141.

PULMONOLOGIST—Southern California. Qualified Pulmonary Internist to join solo certified Pulmonologist in predominantly specialty practice. Attractive location. Contact Pulmonary Position, PO Box 4110, Seal Beach, CA 90740.

PRIMARY CARE—PORTLAND, OREGON. BC/BE. FP, IM, or ER to join dynamic ambulatory care network. Minimum 2 years experience, competitive salary, benefits. Letter/CV to Medical Director, Good Samaritan Immediate Care Centers, PO Box 23608, Tigard, OR 97223.

MEDICAL DIRECTOR—Emanuel Hospital, Portland, Oregon, is seeking board certified MD applicants for a Medical Director to oversee the medical management of this tertiary facility. The position has been vacant for four years and will require a dynamic, goal oriented individual willing to create a positive environment for medical practice in a highly competitive market. Emanuel operates a level one trauma center, air ambulance, acute rehabilitation facility, regional burn center, and has a major commitment to women's and children's medicine, cardiology and oncology. Contact: Search Committee, c/o Robert Forman, Vice President, Human Resources, Emanuel Hospital, 2801 N. Gantenbein, Portland, OR 97227. Member HealthLink and Health Network of America. Equal Opportunity Employer.

ORTHOPAEDICS—Private practice opportunity in Espanola, New Mexico. Financial assistance with income guarantee. Easy access to all forms of recreation—just 20 miles north of Santa Fe. For further information, please submit CV to: Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666; or, call 1-800-545-4030, Ext. 8300.

BOARD CERTIFIED FAMILY PHYSICIAN OR GENERAL INTERNIST needed for multispecialty group in Durango, Colorado; Contact Bonnie DuPuis, PO Box 2637, Durango, CO 81302 or Call (303) 247-2611.

PACIFIC NORTHWEST: Beautiful Coeur d'Alene, Idaho, the capital of the Inland Northwest's extensive network of pristine lakes, is in immediate need of a staff physician to join Group Health Northwest, a family practice staff model HMO, now expanding into North Idaho. Excellent benefit package, association with the 24 physicians of Group Health of Spokane, adequate call sharing, vacation and CME coverage, but with the independence of a small practice in a beautiful lakeside town which has a hospital and most specialties represented. Board certified FP's with OB experience desired. Contact Thomas Kearney, Group Health of North Idaho, PO Box 5339, Coeur d'Alene, ID 83814.

CARDIOLOGIST, INVASIVE—150-physician, multispecialty, prepaid group located in the San Francisco Bay Area wishes to add another Cardiologist/Internist. Practice includes large volume of referrals for invasive procedures. Doppler-echo skills required. University affiliation available. Please contact: E. Andrews Neal, MD, The Permanente Medical Group, Inc., 260 International Circle, San Jose, CA 95119; Telephone (408) 972-6340.

FEMALE FAMILY PRACTITIONER needs partner. Temporary or permanent. Must enjoy women and children and be open to alternatives. PO Box 819, Mendocino, CA 95460; (707) 937-4272.

FAMILY PRACTICE at scenic Lake Chelan, Washington. Join 3 other FP's in a busy rural vacation paradise. Obstetrics required. Salary first year with opportunity to establish your own private practice. Modern local 30 bed hospital with close by regional medical referral center. Lake Chelan is the Gateway to Stehekin and the North Cascade National Park. Position available October 1986. Write Lake Chelan Clinic, PO Box 368, Chelan, WA 98816 or call (509) 682-2511.

PHYSICIAN COORDINATOR, Emergency Department/Prompt Care Center, Saint Cabrini Hospital of Seattle. This private 189-bed facility in the heart of Seattle is looking for a dynamic physician to serve as an Emergency Physician and Coordinator of our Emergency Department and Prompt Care Center. This hospital, while providing general surgical and medical care, is focusing on specialized services such as in- and outpatient psychiatric program, an inpatient advance eatings disorders treatment program, extensive laser treatment service, a comprehensive program on older adult care services on both an inpatient and outpatient basis, emergency department services and prompt care center. We are looking for a physician with strong leadership capabilities, planning and healthcare system expertise and recent emergency medicine experience. Family practice board eligibility or certification preferred. Please submit your résumé to: Ronald C. M. Bergstrom, Administrator, Saint Cabrini Hospital, Terry & Madison, Seattle, WA 98104.

RADIATION ONCOLOGIST—BC/BE to be Director for newly established radiation treatment center in a private practice setting. Excellent terms with guarantee and incentive plan. Submit CV to: Alfred G. Robinson, MD, 867 W. Lancaster Blvd., Lancaster, CA 93534; (805) 948-5928.

80-MEMBER MULTISPECIALTY GROUP seeking two Board certified or eligible Family Practice physicians for openings in satellite offices in Ceres and Patterson. Generous first year guarantee with incentives based on productivity. Excellent fringe benefits including malpractice, retirement, health/dental insurance. Located in Northern California within 2 hours of San Francisco, Yosemite, Sierra Mountains, Carmel. Send CV with references to: C. R. Maino, MD, Gould Medical Foundation, 600 Coffee Road, Modesto, CA 95355.

BEAUTIFUL MOUNTAINOUS MONTANA—Family Physician needed in rural setting to help staff small hospital. Full spectrum practice. Outdoor activities and recreation abound including fishing, hunting, skiing, etc. Hot springs located in town. Guarantees provided. Opening for fall of 1986. Send CV to: Mountainview Clinic, PO Box 469, White Sulphur Springs, MT 59645, or call (406) 547-3384.

FAMILY PRACTICE. Immediate part-time/full-time. Well-established three doctor group in prime location across from busy 200 bed hospital. Contact David Dudley or Doctors Cogar, Marlow, or Wade. 200 N. Jackson Ave., San Jose, CA 95116; (408) 251-1010

CALIFORNIA, ORANGE COUNTY: Full-time and part-time positions available in 2 urgent care/family practice centers. Guaranteed minimum with generous benefit package. Potential profitsharing and partnership for exceptional physician. Send CV to Medical Director, 18582 Beach Blvd., #23, Huntington Beach, CA 92648.

PRACTICE YOUR MEDICAL SKILLS in a new clinic in Central California adjacent to ski resort, hi-desert, and ocean. Prefer General Practitioner with Gynecology background. Salary negotiable. Please repy to Number 137, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PHYSICIANS WANTED

RESEARCH ASSOCIATE. Will conduct functional T cell assays for R&D Dept. involving generating and expanding T cell lines and producing T cell clones. Involves developing and validating T cell functional assays. Will also generate monoclonal antibodies directed against functional T cell subsets. Will also participate in selected research and methods development projects in tissue-related areas. Requires MS degree in Immunology or Cell Biology plus 2 years experience in cell culture techniques in academic or industrial laboratory. $29,600/year, 40 hour/week. Place of employment and interviews: Mountain View, CA. Send this ad and a résumé to Job No. CP3801, PO Box 9560, Sacramento, CA 95823-0560 not later than August 6, 1986. EOE.

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Well-established and successful HMO is seeking Specialists and Primary Care physicians for our facilities in Los Angeles and Orange Counties. Located in close proximity to major teaching centers, we offer the opportunity for continued professional development and rewarding clinical practice. Excellent compensation and benefits package, including profit sharing. Please send CV to:

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FAMILY PRACTICE opportunity to join established practitioner in San Diego area, computerized, dynamic growing practice, call shared large group needs BC/BE personable. (619) 579-8202 ask for Pam Smart.

GENERAL AND PERIPHERAL VASCULAR SURGEON BC/BE to join solo practitioner in Pacific Northwest, population 130,000, three hospitals, excellent surgical and anesthesia facilities, easy access to year 'round outdoor activities. Please send CV to Number 138, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

HEALDSBURG (SONOMA COUNTY) (60 miles North of San Francisco). Medical Director for Maternal Child Health and Rural Health Clinics. Full-time, medical/administrative duties. Bilingual, English/Spanish highly desirable. Board certified. Competitive salary and benefit package, malpractice insurance. Send CV to Alejandra Holmes, Exec. Director, 619 Center St., Healdsburg, CA 95448; (707) 433-6603.

IMMEDIATE OPPORTUNITY available for Family Practice Physician, Board eligible/certified to join five physician multispecialty group. Excellent patient population, well equipped clinic with first year salary guaranteed. Excellent fringe benefits. Affiliated with 60 bed community hospital, teaching opportunities available. Conveniently located in scenic, recreational area with close proximity to La Crosse, Wisconsin. Please send curriculum vitae to R. A. Starr, MD, 318 West Decker St., Viroqua, WI 54665; (608) 637-3175 or (608) 637-3177.

IDAHO NEEDS FULL-TIME EMERGENCY PHYSICIAN. 20 miles from Boise, near mountains and unlimited recreation. Excellent opportunity to affiliate with 162 bed hospital. ACLS-Yes. Contact M. Kutsurelis, Sr. Vice President, Mercy Medical Center, 1512 12th Avenue Rd., Nampa, ID 83651; (208) 467-1171.

OBSTETRICIAN-GYNECOLOGIST: Immediate opening for Board certified/eligible OB/GYN with comprehensive women's health care practice. Multispecialty group includes OB/GYN, Internal Medicine, Family Practice, Clinical Psychologist, and Nurse Practitioners. Stanford University and community hospital affiliations. Located in Palo Alto, a prestigious community 45 minutes from San Francisco. Excellent salary and benefit package leading to full association offered. Malpractice paid. Reply with CV to Judith Ashenfelter, Administrator, 770 Welch Rd., #150, Palo Alto, CA 94304; (415) 327-4051.

PHYSICIANS WANTED

BOARD CERTIFIED OR FACS TO ASSIST AT SURGERY WITH

prospect of joining nationally recognized hernia institute in Beverly Hills. Write with CV to: Lichtenstein Hernia Institute, 9201 Sunset Blvd., Suite 505, Los Angeles, CA 90069.

HEALDSBURG (SONOMA COUNTY) (60 miles North of San Francisco). Physician for rural health clinic, part-time or full-time, OB, Family. English/Spanish highly desirable. Competitive salary and benefit package. Malpractice insurance. Send CV to: Alejandra Holmes, Exec. Director, 619 Center St., Healdsburg, CA 95448; (707) 433-6603.

NORTHERN SAN FRANCISCO BAY AREA—Seeking physician Board certified or eligible in Internal Medicine for internist position in growing department of medicine. Competitive salary and excellent benefits. Call or write: Chief, Dept. of Medicine, Kaiser Permanente Medical Center, 1550 Gateway Blvd., Fairfield, CA 94533; (707) 427-4200.

OREGON OPPORTUNITY—Portland group looking for two new partners. Solid growing practice. First year guarantee plus benefits. Contact: The Friedrich Group, Inc., 9284 Ferncliff NE, Bainbridge Island, WA 98110; (206) 842-5248.

OB/GYN ASSOCIATE REQUIRED—San Diego, California. Excellent opportunity to join established, successful OB/GYN practice, in San Diego, California. Busy Physician needs associate for 22-year-old practice, netting $320,000/year. Located in prime location with emphasis on infertility, gynecological surgery, PMS, minimal OB. Fully equipped office, in central location within minutes of three hospitals. For details call (619) 276-9636, Attn: C. Meyers, or send CV to: 4501 Mission Bay Dr., Ste. 1E, San Diego, CA 92109, Attn: C. Meyers.

FAMILY PRACTITIONER for small active medical group of five Internists/specialists in Southern California, west Riverside County; 30 minutes from Orange County. Competitive salary with bonus plan. Malpractice insurance paid. Position available August '86. Send CV to Number 139, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

SANTA BARBARA—Santa Barbara County Health Care Services position available September, 1986, for Deputy Director, Public Health Services. Reporting directly to the Agency Director, this executive position is responsible for overall functioning of Public Health Services. Requires valid CA license as a physician and surgeon and three years clinical experience as a physician, including one year in an administrative capacity. Prefer person with strong leadership, planning, organizational, and staff development skills to coordinate administrative and medical programs and personnel. Salary $77,508/year plus excellent benefits. Open until filled. Obtain County application and supplemental questionnaire from: Santa Barbara County Personnel Department, 1226 Anacapa St., Santa Barbara, CA 93101; (805) 963-7155; AA/EOE.

NORTHWEST WASHINGTON—One or two Family Practitioners needed and General Surgeon with trauma/vascular interest, Board certified. Five GPs retiring. Ideal setting, close to mountains and San Juan Islands. Contact: Administrator, North Cascade Professional Park, 1916 Hospital Dr., Sedro Woolley, WA 98284; (206) 856-4522.

FAMILY PRACTITIONER—Locum available in a well established Berkeley practice with two other practitioners. Permanent practice opportunity possible. Would like start date August (September or October okay). Locum ends mid-March 1987. Please call Dr Rosenman at (415) 540-8200.

PHYSICIANS WANTED

FAMILY PRACTICE PHYSICIAN NEEDED

Tulare District Hospital seeks certified or eligible FP physician as associate in existing private practice. Excellent opportunity—guarantee. Central California's San Joaquin Valley offers superior lifestyle, family environment, outdoor recreation. Growing community, 75,000 service area population. 112 bed hospital, excellent ancillary services. Please send CV or call:

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FAMILY PHYSICIAN for growing innovative family health center in San Francisco Bay Peninsula. Practice OB and newborn to geriatrics. No major surgery. Health education emphasis. Multidisciplinary team. POMR. Abundant education and teaching opportunity. Ideal living. ABFP certified, residency preferred. Women applicants encouraged. EOE. Salary negotiable. Contact: J. Hopkins, MD, 704 Webster, Palo Alto, CA 94301; (415) 324-1940.

EXCELLENT PRIVATE PRACTICE opportunity in this small but growing beautiful mountain resort community 90 miles north of Los Angeles. Young solo Internist with a very busy and rapidly growing patient oriented practice seeks a competent, motivated and caring Internist. Partnership is the goal. Generous starting salary. Send CV to Terry Warsaw, MD, 29912 Greenwater Dr., Tehachapi, CA 93561.

PHYSICIANS WANTED

PHYSICIAN I, Student Health Center, California ($4,792-$5,772/mo.; full-time/10 months). Primary care physician to work with six other generalists in unique program and operation in a university health setting in desirable area. Completion of one year internship and/or equivalent postgraduate year of training in practice of medicine required. CV and application due by July 16, 1986. Apply Personnel Office, Cal Poly, San Luis Obispo, CA 93407; (805) 546-2236. AA/EOE/Title IX/Rehabilitation Act of 1973 Employer.

STUDENT HEALTH PHYSICIAN, Sonoma State University (Northern California). As part of staff of three physicians, provides general out-patient care at a California State University campus. Salary range: $4,792-$5,772/month; potential increase based on legislative action. Apply by July 25, 1986. Prompt reply appreciated. Starts August 18, 1986. Direct résumé with cover letter or inquiries to Personnel Office, SSU, Rohnert Park, CA 94928. Applications are also being taken on a continuing basis for a temporary physician pool. For more information, call (707) 664-2166 (voice), (707) 664-2751 (TDD). AA-EO Employer.

GENERAL INTERNIST—General Internist with an emphasis on cardiology. Is this important to you? Pacific Northwest life-style, prime urban location, with specialty group setting, private practice, excellent benefit, and first year salary guarantee with incentives. Send your curriculum vitae or call: The Friedrich Group, Inc., 9284 Ferncliff Northeast, Bainbridge Island, WA 98110; (206) 842-5248 or 527-3141.

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CALIFORNIA PRACTICES FOR SALE. All specialties available. Confidentiality maintained. Request free monthly publication. Appraisals. Financing. Contact PSL (714) 771-4331; (213) 934-0515; (619) 234-9515.

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INTERNIST, Hematology/Oncology subspecialty, desires position with group or HMO Los Angeles County or Orange County, California. David Dworkin, MD, FACP, 6250 Majorca Circle, Long Beach CA 90803; (213) 498-7233.

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(Continued on Page 141)

(Continued from Page 139)

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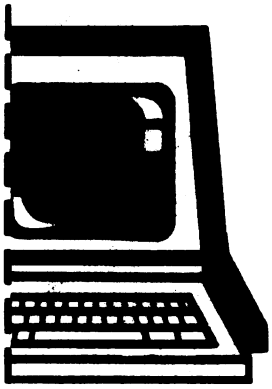

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In depression and anxiety

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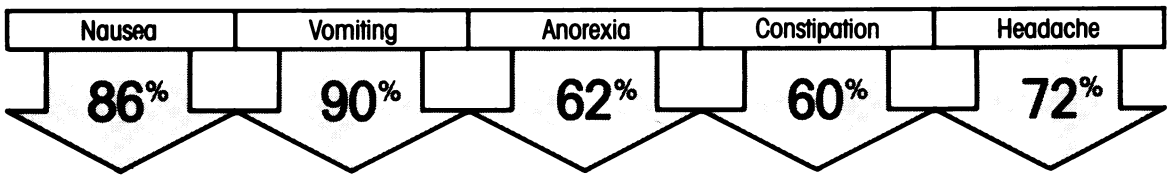
OVERNIGHT—SLEEP IMPROVED[1]

Sleep improved in 74% after only one *h.s.* dose in selected patients

FIRST WEEK—OTHER SOMATIC SYMPTOMS MARKEDLY REDUCED[1]



FOURTH WEEK—PATIENT COMPLIANCE WAS BETTER[2]

More than three times as many amitriptyline patients as Limbitrol patients dropped out of therapy because of side effects, although the incidence of side effects was similar. Caution patients against the combined effects of Limbitrol with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as operating machinery or driving a car. In general, limit dosage to lowest effective amount in elderly patients.

References: 1. Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 2. Feighner JP, *et al: Psychopharmacology 61*:217-225, Mar 22, 1979.

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓥ

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) Ⓥ

A brighter perspective...sooner

Limbitrol® Ⓥ Tranquilizer–Antidepressant

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.

Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving).

***Usage in Pregnancy:* Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs. Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:

Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.

Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.

Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly.

Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.

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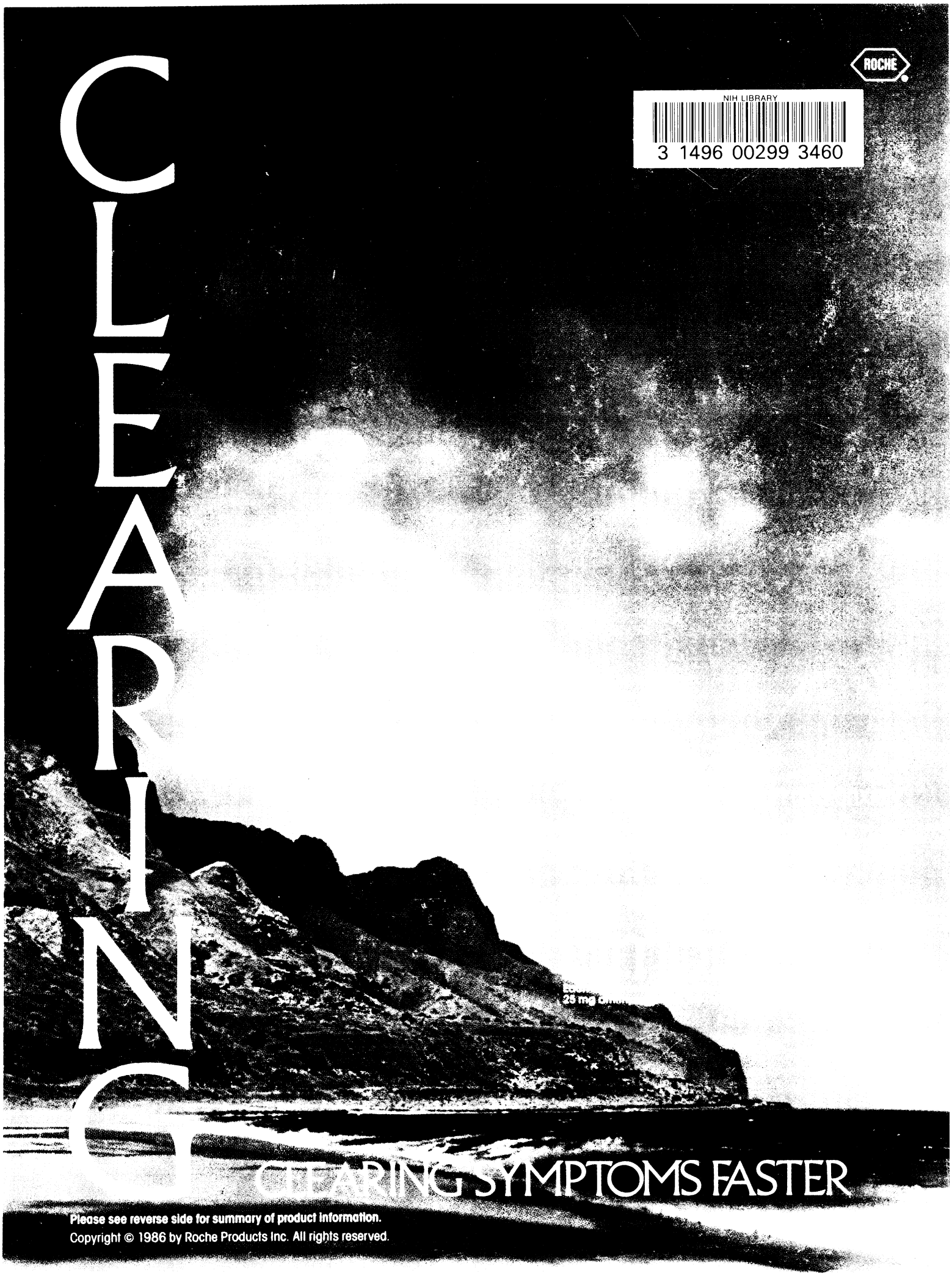

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