XANAX RELIEVES CLINICAL ANXIETY WITH DEPRESSIVE SYMPTOMS.

XANAX, the first triazolobenzodiazepine, is characterized by a structure uniquely different from other benzodiazepines.

In addition to effectively relieving clinical anxiety, XANAX Tablets have been found to be significantly more effective ($p<0.001$) than placebo in decreasing depressed mood score (HARS) in patients with clinical anxiety.*

A DESIRABLE PROFILE OF CLINICAL ADVANTAGES

- **Intermediate half-life** of 12 to 15 hours
- **Significantly lower incidence of drowsiness** when compared directly with diazepam in clinical studies*
- **No greater incidence of anticholinergic effects** than with placebo, eg, dry mouth, constipation, tremor†
- **No reports of symptomatic postural hypotension or cardiovascular toxicity**†
- **Documented 16-week effectiveness** with no appreciable increase in dosage from week 4 to week 16†
- **Simple dosage**—0.25 to 0.5 mg t.i.d.

*Cohn JB: J *Clin Psychiatry* 42(9):347-351, 1981.
†Data on file, The Upjohn Company.

Xanax® 0.5 mg Tablets

alprazolam C IV

Upjohn The Upjohn Company Kalamazoo, Michigan 49001

Please see next page for brief summary of prescribing information.

XANAX® Tablets ©
(alprazolam)

CONTRAINDICATIONS
Patients with sensitivity to this drug or other benzodiazepines and in acute narrow angle glaucoma.

WARNINGS
Not of value in psychotic patients. Caution patients against hazardous occupations requiring complete mental alertness and about the simultaneous ingestion of alcohol and other CNS depressant drugs.

Benzodiazepines can cause fetal harm in pregnant women. Warn patients of the potential hazard to the fetus. Avoid during the first trimester.

PRECAUTIONS
General: If XANAX is combined with other psychotropics or anticonvulsant drugs, consider drug potentiation. Exercise the usual precautions regarding size of the prescription for depressed or suicidal patients. In elderly and debilitated patients, use the lowest possible dosage. Observe the usual precautions in treating patients with impaired renal or hepatic function.

Information for Patients: Alert patients about: (a) consumption of alcohol and drugs, (b) possible fetal abnormalities, (c) operating machinery or driving, (d) not increasing dose of the drug due to risk of dependence, (e) not stopping the drug abruptly. *Laboratory Tests:* Not ordinarily required in otherwise healthy patients. *Drug Interactions:* Additive CNS depressant effects with other psychotropics, anticonvulsants, antihistamines, ethanol and other CNS depressants. Pharmacokinetic interactions with benzodiazepines have been reported. *Drug/Laboratory Test Interactions:* No consistent pattern for a specific drug or specific test. *Carcinogenesis, Mutagenesis, Impairment of Fertility:* No carcinogenic potential or impairment of fertility in rats. *Pregnancy:* See Warnings. *Nonteratogenic Effects:* The child born of a mother on benzodiazepines may be at some risk for withdrawal symptoms and neonatal flaccidity. *Labor and Delivery:* No established use. *Nursing Mothers:* Benzodiazepines are excreted in human milk. Women on XANAX should not nurse. *Pediatric Use:* Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS
Side effects are generally observed at the beginning of therapy and usually disappear with continued medication. In the usual patient, the most frequent side effects are likely to be an extension of the pharmacological activity of XANAX, e.g., drowsiness or lightheadedness.

Central Nervous System: Drowsiness, lightheadedness, depression, headache, confusion, insomnia, nervousness, syncope, dizziness, akathisia, and tiredness/sleepiness.

Gastrointestinal: Dry mouth, constipation, diarrhea, nausea/vomiting, and increased salivation.

Cardiovascular: Tachycardia/palpitations, and hypotension.

Sensory: Blurred vision.

Musculoskeletal: Rigidity and tremor.

Cutaneous: Dermatitis/allergy.

Other Side Effects: Nasal congestion, weight gain, and weight loss.

In addition, the following adverse events have been reported with the use of anxiolytic benzodiazepines: dystonia, irritability, concentration difficulties, anorexia, loss of coordination, fatigue, sedation, slurred speech, jaundice, musculoskeletal weakness, pruritus, diplopia, dysarthria, changes in libido, menstrual irregularities, incontinence and urinary retention.

Paradoxical reactions such as stimulation, agitation, increased muscle spasticity, sleep disturbances, and hallucinations may occur. Should these occur, discontinue the drug.

During prolonged treatment, periodic blood counts, urinalysis, and blood chemistry analyses are advisable. Minor EEG changes, of unknown significance, have been observed.

DRUG ABUSE AND DEPENDENCE
Physical and Psychological Dependence: Withdrawal symptoms have occurred following abrupt discontinuance of benzodiazepines. After prolonged therapy, dosage should be tapered. *Controlled Substance Class:* XANAX is a controlled substance and has been assigned to schedule IV.

CAUTION: FEDERAL LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION. BS-1

Upjohn THE UPJOHN COMPANY
Kalamazoo, Michigan 49001 USA

J-9946 September 1982

For Irritable Bowel Syndrome

Each Extentab contains:

Phenobarbital, USP (¾ gr)	48.6 mg
(Warning: May be habit forming)	
Hyoscyamine Sulfate, USP	0.3111 mg
Atropine Sulfate, USP	0.0582 mg
Scopolamine Hydrobromide, USP	0.0195 mg

The following is a brief summary only. Before prescribing, see complete prescribing information in Donnatal Extentabs product labeling or PDR.

INDICATIONS

Based on a review of this drug by the National Academy of Sciences — National Research Council and/or other information, FDA has classified the following indications as "possibly" effective:

For use as adjunctive therapy in the treatment of irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

May also be useful as adjunctive therapy in the treatment of duodenal ulcer. IT HAS NOT BEEN SHOWN CONCLUSIVELY WHETHER ANTICHOLINERGIC / ANTISPASMODIC DRUGS AID IN THE HEALING OF A DUODENAL ULCER, DECREASE THE RATE OF RECURRENCES OR PREVENT COMPLICATIONS.

Contraindications: Glaucoma; obstructive uropathy; obstructive disease of the G.I. tract; paralytic ileus; intestinal atony; unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis especially if complicated by toxic megacolon; myasthenia gravis; hiatal hernia associated with reflux esophagitis; hypersensitivity to any of the ingredients; acute intermittent porphyria.

Warnings: In the presence of a high environmental temperature, heat prostration can occur.

Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance, treatment with this drug would be inappropriate and possibly harmful.

Donnatal may produce drowsiness or blurred vision.

Phenobarbital may decrease the effect of anticoagulants.

Phenobarbital may be habit forming.

Initial doses should be small in patients with hepatic dysfunction.

Precautions: Use with caution in patients with autonomic neuropathy, hepatic or renal disease, hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmais, tachycardia, and hypertension.

Belladonna alkaloids may produce a delay in gastric emptying (antral stasis) which would complicate the management of gastric ulcer.

Carcinogenesis, mutagenesis. Long-term studies in animals have not been performed to evaluate carcinogenic potential.

Pregnancy Category C. Animal reproduction studies have not been conducted. Donnatal should be given to pregnant women only if clearly needed.

Nursing mothers. It is not known whether this drug is excreted in human milk, and caution should be exercised when Donnatal is administered to a nursing mother.

Adverse Reactions: May include xerostomia; urinary hesitancy and retention; blurred vision; tachycardia; palpitation; mydriasis; cycloplegia; increased ocular tension; loss of taste sense; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; musculoskeletal pain; severe allergic reactions such as anaphylaxis, urticaria and other dermal manifestations; decreased sweating. Elderly patients may react with symptoms of excitement, agitation, drowsiness, and other untoward manifestations to even small doses of the drug.

Phenobarbital may produce excitement in some patients. Abrupt withdrawal, in addicts, may cause delirium or convulsions.

Dosage and Administration: The usual dose is one Extentab every twelve (12) hours. If indicated, one Extentab every eight (8) hours may be given.

How Supplied: Pale green coated tablets, monogrammed "AHR" and "DONNATAL EXTENTAB" in bottles of 100 (NDC 0031-4235-63) and 500 (NDC 0031-4235-70) and Dis-Co® Unit Dose Packs of 100 (NDC 0031-4235-64). Rev. Feb. 1981

AHR DONNATAL EXTENTAB

A·H·ROBINS

Pharmaceutical Division
Richmond, Va. 23261-6609
Member of Certified Medical Representatives Institute

Donnatal Extentabs®

B.I.D.

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Sudafed® S.A.
(pseudoephedrine HCl) 120 mg capsules

Sustained action for potent 12-hour relief

Not recommended for children under 12 years of age

Available without Rx in packages of 10s and 40s

And remember the rest of the family...

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Sudafed® Syrup
(pseudoephedrine HCl), a tasty raspberry-flavored syrup containing 30 mg per 5 cc

Sudafed® Cough Syrup
(pseudoephedrine HCl) containing 30 mg per 5 cc

Potent relief without drowsiness

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The Journal of the American Osteopathic Association
February 1983/Volume 82, Number 6

Cover. Bone marrow aspirate demonstrating the reappearance of mature polymorphonuclear leukocytes following successful treatment with cyclophosphamide.

A report of a case of idiopathic autoimmune neutropenia treated with cyclophosphamide begins on page **419/115.**

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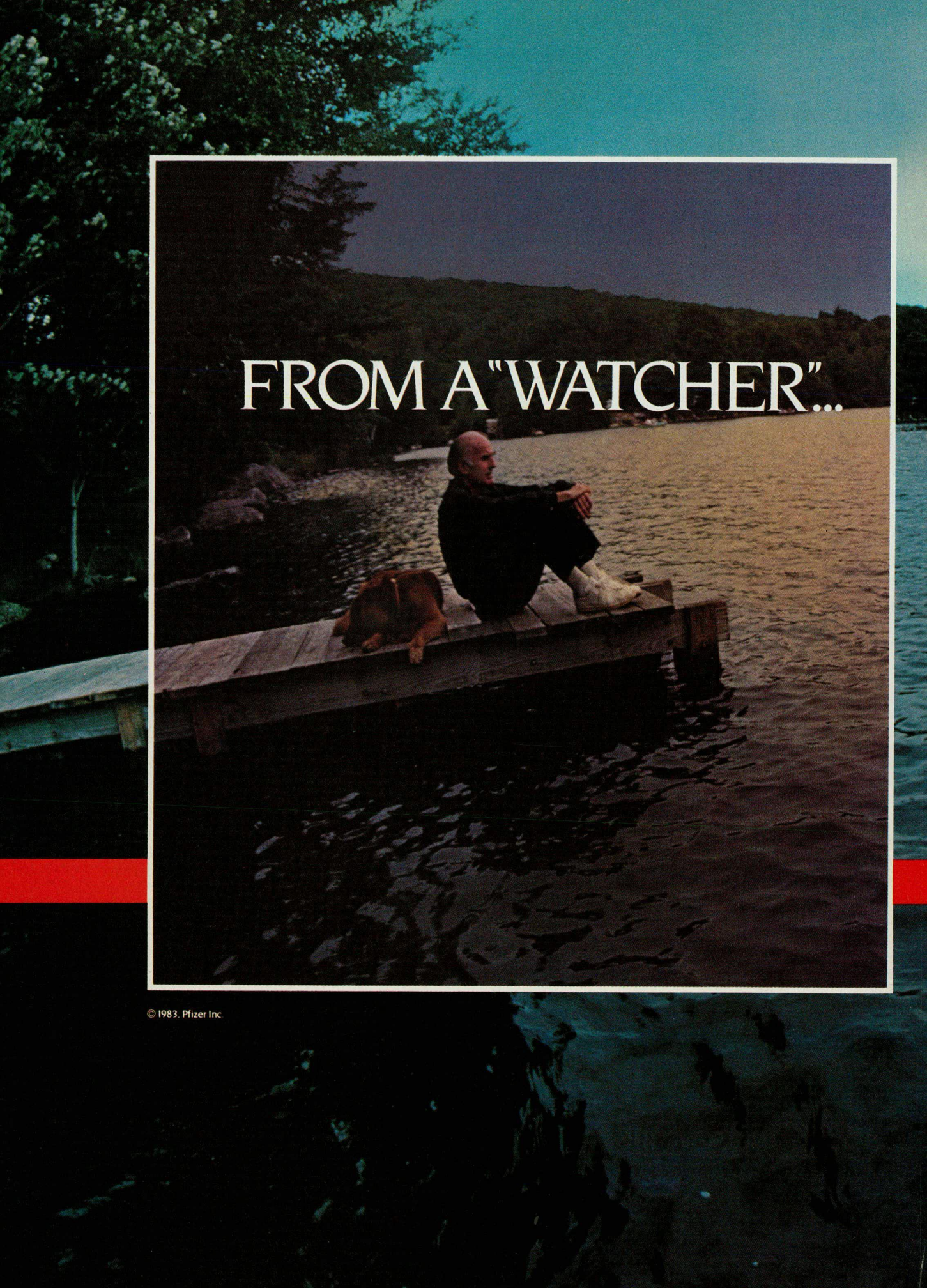

Your angina patients* can become more active now...with PROCARDIA protection. They'll be pain-free more of the time[1] and find their need for nitroglycerin greatly reduced.[2] They'll be able to work harder, exercise more.[3] And be more active participants in their own lives once again.

feeling better...doing more

PROCARDIA®
(NIFEDIPINE) *Capsules 10 mg*

*Procardia is indicated for the management of:

- Confirmed vasospastic angina.
- Angina where the clinical presentation suggests a possible vasospastic component.
- Chronic stable angina without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or nitrates or who cannot tolerate these agents. In chronic stable angina (effort-associated angina) Procardia has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in these patients are incomplete.

Please see PROCARDIA® *brief summary on next page*

feeling better...doing more

PROCARDIA®
(NIFEDIPINE) *Capsules 10 mg*

–Usual effective dosage is 30-60 mg/day

For most patients, titrate over 7 to 14 days, using the patient's blood pressure response, attack frequency, sublingual nitroglycerin intake and activity level as a guide. Titration may be more rapid (e.g., 3 days) if symptoms warrant and the patient is observed closely.

Because Procardia decreases peripheral vascular resistance, careful monitoring of blood pressure during initial administration and titration is suggested. Close observation is especially recommended for patients taking medication known to lower blood pressure.

–Offers a favorable safety profile

Most frequently reported side effects, usually mild, are dizziness or lightheadedness, peripheral edema, nausea, weakness, headache and flushing, each occurring in about 10% of patients, transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%.

References:

1. Stone PH, Turi ZG, Muller JE: Efficacy of nifedipine therapy for refractory angina pectoris. *Am Heart J* 104:672-681, September 1982.
2. Antman E, Muller J, Goldberg S, el al: Nifedipine therapy for coronary-artery spasm: Experience in 127 patients. *N Eng J Med* 302:1269-1273, June 5, 1980.
3. De Ponti C, De Biase AM, Pirelli S, et al: Effects of nifedipine, acebutolol, and their association on exercise tolerance in patients with effort angina. *Cardiology* 68 (suppl 2): 195-199, 1981.

BRIEF SUMMARY
PROCARDIA® CAPSULES For Oral Use
(nifedipine)

INDICATIONS AND USAGE: I. Vasospastic Angina: PROCARDIA (nifedipine) is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not incompatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. PROCARDIA may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable threshold on exertion or in unstable angina where electrocardiographic findings are compatible with intermittent vasospasm, or when angina is refractory to nitrates and/or adequate doses of beta blockers.

II. Chronic Stable Angina (Classical Effort-Associated Angina): PROCARDIA is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents.

In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in those patients are incomplete.

Controlled studies in small numbers of patients suggest concomitant use of PROCARDIA and beta blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs. (See Warnings.)

CONTRAINDICATIONS: Known hypersensitivity reaction to PROCARDIA.

WARNINGS: Excessive Hypotension: Although in most patients, the hypotensive effect of PROCARDIA is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients on concomitant beta blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients receiving PROCARDIA together with a beta blocking agent who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of PROCARDIA and a beta blocker, but the possibility that it may occur with PROCARDIA alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analgesics cannot be ruled out.

Increased Angina: Occasional patients have developed well documented increased frequency, duration or severity of angina on starting PROCARDIA or at the time of dosage increases. The mechanism of this response is not established but could result from decreased coronary perfusion associated with decreased diastolic pressure with increased heart rate, or from increased demand resulting from increased heart rate alone.

Beta Blocker Withdrawal: Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of PROCARDIA treatment will not prevent this occurrence and might be expected to exacerbate it by provoking reflex catecholamine release. There have been occasional reports of increased angina in a setting of beta blocker withdrawal and PROCARDIA initiation. It is important to taper beta blockers if possible, rather than stopping them abruptly before beginning PROCARDIA.

Congestive Heart Failure: Rarely, patients, usually receiving a beta blocker, have developed heart failure after beginning PROCARDIA. Patients with tight aortic stenosis may be at greater risk for such an event.

PRECAUTIONS: General: Hypotension: Because PROCARDIA decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of PROCARDIA is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. (See Warnings.)

Peripheral edema: Mild to moderate peripheral edema, typically associated with arterial vasodilation and not due to left ventricular dysfunction, occurs in about one in ten patients treated with PROCARDIA. This edema occurs primarily in the lower extremities and usually responds to diuretic therapy. With patients whose angina is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

Drug interactions: Beta-adrenergic blocking agents: (See Indications and Warnings.) Experience in over 1400 patients in a non-comparative clinical trial has shown that concomitant administration of PROCARDIA and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.

Long-acting nitrates: PROCARDIA may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.

Digitalis: Administration of PROCARDIA with digoxin increased digoxin levels in nine of twelve normal volunteers. The average increase was 45%. Another investigator found no increase in digoxin levels in thirteen patients with coronary artery disease. In an uncontrolled study of over two hundred patients with congestive heart failure during which digoxin blood levels were not measured, digitalis toxicity was not observed. Since there have been isolated reports of patients with elevated digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing PROCARDIA to avoid possible over- or under-digitalization.

Carcinogenesis, mutagenesis, impairment of fertility: When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose.

Pregnancy: Category C. Please see full prescribing information with reference to teratogenicity in rats, embryotoxicity in rats, mice and rabbits, and abnormalities in monkeys.

ADVERSE REACTIONS: The most common adverse events include dizziness or light-headedness, peripheral edema, nausea, weakness, headache and flushing each occurring in about 10% of patients, transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%. Syncopal episodes did not recur with reduction in the dose of PROCARDIA or concomitant antianginal medication. Additionally, the following have been reported: muscle cramps, nervousness, dyspnea, nasal and chest congestion, diarrhea, constipation, inflammation, joint stiffness, shakiness, sleep disturbances, blurred vision, difficulties in balance, dermatitis, pruritus, urticaria, fever, sweating, chills, and sexual difficulties. Very rarely, introduction of PROCARDIA therapy was associated with an increase in anginal pain, possibly due to associated hypotension.

In addition, more serious adverse events were observed, not readily distinguishable from the natural history of the disease in these patients. It remains possible, however, that some or many of these events were drug related. Myocardial infarction occurred in about 4% of patients and congestive heart failure or pulmonary edema in about 2%. Ventricular arrhythmias or conduction disturbances each occurred in fewer than 0.5% of patients.

Laboratory Tests: Rare, mild to moderate, transient elevations of enzymes such as alkaline phosphatase, CPK, LDH, SGOT, and SGPT have been noted, and a single incident of significantly elevated transaminases and alkaline phosphatase was seen in a patient with a history of gall bladder disease after about eleven months of nifedipine therapy. The relationship to PROCARDIA therapy is uncertain. These laboratory abnormalities have rarely been associated with clinical symptoms. Cholestasis, possibly due to PROCARDIA therapy, has been reported twice in the extensive world literature.

HOW SUPPLIED: Each orange, soft gelatin PROCARDIA CAPSULE contains 10 mg of nifedipine. PROCARDIA CAPSULES are supplied in bottles of 100 (NDC 0069-2600-66), 300 (NDC 0069-2600-72), and unit dose (10x10) (NDC 0069-2600-41). The capsules should be protected from light and moisture and stored at controlled room temperature 59° to 77°F (15° to 25°C) in the manufacturer's original container.

More detailed professional information available on request.

Pfizer **LABORATORIES DIVISION**
PFIZER INC.