In ACE inhibitors

24-hour power* in blood pressure control

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STUART

...ve effect may diminish at the end of the dosing interval.

...verse side of this advertisement for brief summary of prescribing information.

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INDICATIONS AND USAGE. ZESTRIL is indicated for the treatment of hypertension. It may be used alone as initial therapy or concomitantly with other classes of antihypertensive agents. In using ZESTRIL, consideration should be given to the fact that another angiotensin converting enzyme inhibitor, captopril, has caused agranulocytosis, particularly in patients with renal impairment or collagen vascular disease, and that available data are insufficient to show that ZESTRIL does not have a similar risk. (See WARNINGS.) **CONTRAINDICATIONS.** ZESTRIL is contraindicated in patients who are hypersensitive to this product and in patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor. **WARNINGS. Angioedema:** Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including ZESTRIL. In such cases, ZESTRIL should be promptly discontinued, and the patient carefully observed until the swelling disappears. In instances where swelling has been confined to the face and lips the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. **Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, eg, subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL) should be promptly administered. (See ADVERSE REACTIONS.) Hypotension:** Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of use with ZESTRIL in 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 ZESTRIL and/or diuretic is increased. Similar considerations apply to patients with ischemic heart or cerebrovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. 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, captopril, 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 ZESTRIL are insufficient to show that ZESTRIL does not cause agranulocytosis at similar rates. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered. **PRECAUTIONS. General. Impaired Renal Function:** As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin converting enzyme inhibitors, including ZESTRIL, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death. In hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine may occur. Experience with another angiotensin converting enzyme inhibitor suggests that these increases are usually reversible upon discontinuation of ZESTRIL 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 pre-existing renal vascular disease have developed increases in blood urea nitrogen and serum creatinine, usually minor and transient, especially when ZESTRIL has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction of ZESTRIL and/or discontinuation of the diuretic may be required. **Evaluation of the hypertensive patient should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.) Hyperkalemia:** In clinical trials hyperkalemia (serum potassium greater than 5.7 mEq/L) occurred in approximately 2.2% of hypertensive patients and 4.0% of patients with congestive heart failure. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in approximately 0.1% of hypertensive patients. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with ZESTRIL. (See Drug Interactions.) **Surgery/Anesthesia:** In patients undergoing major surgery or during anesthesia with agents that produce hypotension, ZESTRIL 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 ZESTRIL. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician. **Symptomatic Hypotension:** Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patient 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 their physician. **Hyperkalemia:** Patients should be told not to use salt substitutes containing potassium without consulting their physician. **Neutropenia:** Patients should be told to report promptly any indication of infection (eg, sore throat, fever) which may be a sign of neutropenia. **NOTE:** As with many other drugs, certain advice to patients being treated with ZESTRIL 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 ZESTRIL. The possibility of hypotensive effects with ZESTRIL can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with ZESTRIL. If it is necessary to continue the diuretic, initiate therapy with ZESTRIL at a dose of 5 mg daily, and provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS, and DOSAGE AND ADMINISTRATION.) When a diuretic is added to the therapy of a patient receiving ZESTRIL, an additional antihypertensive effect is usually observed. Studies with ACE inhibitors in combination with diuretics indicate that the dose of the ACE inhibitor can be reduced when it is given with a diuretic. (See DOSAGE AND ADMINISTRATION.) **Indomethacin:** In a study in 36 patients with mild to moderate hypertension where the antihypertensive effects of ZESTRIL alone were compared to ZESTRIL given concomitantly with indomethacin, the use of indomethacin was associated with a reduced effect, although the difference between the two regimens was not significant. **Other Agents:** ZESTRIL has been used concomitantly with nitrates and/or digoxin without evidence of clinically significant adverse interactions. No clinically important pharmacokinetic interactions occurred when ZESTRIL was used concomitantly with propranolol or hydrochlorothiazide. The presence of food in the stomach does not alter the bioavailability of ZESTRIL. **Agents Increasing Serum Potassium:** ZESTRIL attenuates potassium loss caused by thiazide-type diuretics. Use of ZESTRIL with potassium-sparing diuretics (eg, 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 because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. **Lithium:** Lithium toxicity has been reported in patients receiving lithium with drugs which cause elimination of sodium, including ACE inhibitors. Lithium toxicity was usually reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if ZESTRIL is administered concomitantly with lithium. **Carcinogenesis, Mutagenesis, Impairment of Fertility.** There was no evidence of a tumorigenic effect when lisinopril was administered for 105 weeks to male and female rats at doses up to 90 mg/kg/day (about 56 times* the maximum recommended daily human dose) or when lisinopril was administered for 92 weeks to (male and female) mice at doses up to 135 mg/kg/day (about 84 times* the maximum recommended daily human dose). *Based on patient weight of 50 kg. Lisinopril was not mutagenic in the Ames microbial mutagen test with or without metabolic activation. It was also negative in a forward mutation assay using Chinese hamster lung cells. Lisinopril did not produce single strand DNA breaks in an in vitro alkaline elution rat hepatocyte assay. In addition, lisinopril did not produce increases in chromosomal aberrations in an in vitro test in Chinese hamster ovary cells or in an in vivo study in mouse bone marrow. There were no adverse effects on reproductive performance in male and female rats treated with up to 300 mg/kg/day of lisinopril. **Pregnancy. Pregnancy Category C:** Lisinopril was not teratogenic in mice treated on days 6-15 of gestation with up to 1,000 mg/kg/day (625 times the maximum recommended human dose). There was an increase in fetal resorptions at doses down to 100 mg/kg; at doses of 1,000 mg/kg this was prevented by saline supplementation. There was no fetotoxicity or teratogenicity in rats treated with up to 300 mg/kg/day (188 times the maximum recommended dose) of lisinopril at days 6-17 of gestation. In rats receiving lisinopril from day 15 of gestation through day 21 postpartum, there was an increased incidence in pup deaths on days 2-7 postpartum and a lower average body weight of pups on day 21 postpartum. The increase in pup deaths and decrease in pup weight did not occur with maternal saline supplementation. Lisinopril, at doses up to 1 mg/kg/day, was not teratogenic when given throughout the organogenic period in saline supplemented rabbits. Saline supplementation (physiologic saline in place of tap water) was used to eliminate maternotoxic effects and enable evaluation of the teratogenic potential at the highest possible dosage level. The rabbit has been shown to be extremely sensitive to angiotensin converting enzyme inhibitors (captopril and enalapril) with maternal and fetotoxic effects apparent at or below the recommended therapeutic dosage levels in man. Fetotoxicity was demonstrated in rabbits by an increased incidence of fetal resorptions at an oral dose of lisinopril at 1 mg/kg/day and by an increased incidence of incomplete ossification at the lowest dose tested (0.1 mg/kg/day). A single intravenous dose of 15 mg/kg of lisinopril administered to pregnant rabbits on gestation days 16, 21 or 26 resulted in 88% to 100% fetal death. By whole body autoradiography, radioactivity was found in the placenta following administration of labeled lisinopril to pregnant rats, but none was found in the fetuses. **Human Experience:** There are no adequate and well-controlled studies of lisinopril in pregnant women. However, data are available that show drugs of this class cross the human placenta. Because the risk of fetal toxicity with the use the ACE inhibitors has not been clearly defined (see below), lisinopril should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome. Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality. When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed in utero to ACE inhibitors should be closely observed for hypotension, oliguria and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressores as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypertension or the underlying prematurity. Another ACE inhibitor, enalapril, has been removed from the neonatal circulation by peritoneal dialysis and theoretically may be removed by exchange transfusion, although there is no experience with the latter procedure. There is no experience with either of these procedures for removing lisinopril or other ACE inhibitors from the neonatal circulation. **Nursing Mothers:** Milk of lactating rats contains radioactivity following administration of ^{14}C lisinopril. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ZESTRIL is given to a nursing mother. **Pediatric Use:** Safety and effectiveness in children have not been established. **ADVERSE REACTIONS.** ZESTRIL has been found to be generally well tolerated in controlled clinical trials involving 2003 patients and subjects. The most frequent clinical adverse experiences in controlled trials with ZESTRIL were dizziness (6.3%), headache (5.3%), fatigue (3.3%), diarrhea (3.2%), upper respiratory symptoms (3.0%), and cough (2.9%), all of which were more frequent than in placebo-treated patients. 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 could not be related to total daily dosage within the recommended therapeutic dosage range. For adverse experiences which occurred in more than 1% of patients and subjects treated with ZESTRIL or ZESTRIL plus hydrochlorothiazide in controlled clinical trials, comparative incidence data are listed in the table below.

Percent of Patients in Controlled Studies

	ZESTRIL (n = 2003†) Incidence (discontinuation)	ZESTRIL/Hydrochlorothiazide (n = 644) Incidence (discontinuation)	Placebo (n = 207) Incidence
Dizziness	6.3 (0.6)	9.0 (0.9)	1.9
Headache	5.3 (0.2)	4.3 (0.5)	1.9
Fatigue	3.3 (0.2)	3.9 (0.5)	1.0
Diarrhea	3.2 (0.3)	2.6 (0.3)	2.4
Upper Respiratory Symptoms	3.0 (0.0)	4.5 (0.0)	0.0
Cough	2.9 (0.4)	4.5 (0.8)	1.0
Nausea	2.3 (0.3)	2.5 (0.2)	2.4
Hypotension	1.8 (0.8)	1.6 (0.5)	0.5
Rash	1.5 (0.4)	1.6 (0.2)	0.5
Orthostatic Effects	1.4 (0.0)	3.4 (0.2)	1.0
Asthenia	1.3 (0.4)	2.0 (0.2)	1.0
Chest Pain	1.3 (0.1)	1.2 (0.2)	1.4
Vomiting	1.3 (0.2)	1.4 (0.0)	0.5
Dyspnea	1.1 (0.0)	0.5 (0.2)	1.4
Dyspepsia	1.0 (0.0)	1.9 (0.0)	0.0
Paresthesia	0.8 (0.0)	2.0 (0.2)	0.0
Impotence	0.7 (0.2)	1.6 (0.3)	0.0
Muscle Cramps	0.6 (0.0)	2.8 (0.6)	0.5
Back Pain	0.5 (0.0)	1.1 (0.0)	1.4
Nasal Congestion	0.3 (0.0)	1.2 (0.0)	0.0
Decreased Libido	0.2 (0.1)	1.2 (0.0)	0.0
Vertigo	0.1 (0.0)	1.1 (0.2)	0.0

†Includes 420 patients treated for congestive heart failure who were receiving concomitant digitalis and/or diuretic therapy.

Clinical adverse experiences occurring in 0.3% to 1.0% of patients in the controlled trials and rarer, serious, possibly drug related events reported in uncontrolled studies or marketing experience included: BODY AS A WHOLE: Chest discomfort, fever, flushing. CARDIOVASCULAR: Angina pectoris, orthostatic hypotension, rhythm disturbances, tachycardia, peripheral edema, palpitation. DIGESTIVE: Abdominal pain, anorexia, constipation, flatulence. METABOLISM: Gout. MUSCULOSKELETAL: Joint pain, shoulder pain. NERVOUS SYSTEM/PSYCHIATRIC: Depression, somnolence, insomnia, stroke. RESPIRATORY SYSTEM: Bronchitis, sinusitis, pharyngeal pain. UROGENITAL: Oliguria, progressive azotemia, acute renal failure. OTHER: Blurred vision, pruritus, urinary tract infection, vasculitis of the legs. ANGIOEDEMA: Angioedema has been reported in patients receiving ZESTRIL (0.1%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis and/or larynx occurs, treatment with ZESTRIL should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.) HYPOTENSION: In hypertensive patients, hypotension occurred in 1.2% and syncope occurred in 0.1% of patients. Hypotension or syncope was a cause of discontinuation of therapy in 0.5% of hypertensive patients. (See WARNINGS.) In patients with congestive heart failure, hypotension occurred in 5.0% and syncope occurred in 1.0% of patients. These adverse experiences were causes for discontinuation of therapy in 1.3% of these patients. **Clinical Laboratory Test Findings. Serum Electrolytes:** 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 2.0% of patients with essential hypertension treated with ZESTRIL alone. Increases were more common in patients receiving concomitant diuretics and in patients with renal artery stenosis. (See PRECAUTIONS.) Reversible minor increases in blood urea nitrogen and serum creatinine were observed in approximately 9.1% of patients with congestive heart failure on concomitant diuretic therapy. Frequently, these abnormalities resolved when the dosage of the diuretic was decreased. **Hemoglobin and Hematocrit:** Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.4 g% and 1.3 vol%, respectively) occurred frequently in patients treated with ZESTRIL but were rarely of clinical importance in patients without some other cause of anemia. 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. Overall, 2.0% of patients discontinued therapy due to laboratory adverse experiences, principally elevations in blood urea nitrogen (0.6%), serum creatinine (0.5%), and serum potassium (0.4%). **OVERDOSAGE.** The oral LD_{50} of lisinopril is greater than 20 g/kg in mice and rats. The most likely manifestation of overdosage would be hypotension, for which the usual treatment would be intravenous infusion of normal saline solution. Lisinopril can be removed by hemodialysis. **DOSAGE AND ADMINISTRATION. Initial Therapy:** In patients with uncomplicated essential hypertension not on diuretic therapy, the recommended initial dose is 10 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 20-40 mg per day administered in a single daily dose. The antihypertensive effect may diminish toward the end of the dosing interval regardless of the administered dose, but most commonly with a dose of 10 mg daily. This can be evaluated by measuring blood pressure just prior to dosing to determine whether satisfactory control is being maintained for 24 hours. If it is not, an increase in dose should be considered. Doses up to 80 mg have been used but do not appear to give greater effect. If blood pressure is not controlled with ZESTRIL alone, a low dose of a diuretic may be added. Hydrochlorothiazide, 12.5 mg has been shown to provide an additive effect. After the addition of a diuretic, it may be possible to reduce the dose of ZESTRIL. **Diuretic Treated Patients:** In hypertensive patients who are currently being treated with a diuretic, symptomatic hypotension may occur occasionally following the initial dose of ZESTRIL. The diuretic should be discontinued, if possible, for two to three days before beginning therapy with ZESTRIL to reduce the likelihood of hypotension. (See WARNINGS.) The dosage of ZESTRIL should be adjusted according to blood pressure response. If the patient's blood pressure is not controlled with ZESTRIL alone, diuretic therapy may be resumed as described above. If the diuretic cannot be discontinued, an initial dose of 5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) Concomitant administration of ZESTRIL with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium. (See PRECAUTIONS.) **Use in Elderly:** In general, blood pressure response and adverse experiences were similar in younger and older patients given similar doses of ZESTRIL. Pharmacokinetic studies, however, indicate that maximum blond levels and area under the plasma concentration time curve (AUC) are doubled in older patients so that dosage adjustments should be made with particular caution. **Dosage Adjustment in Renal Impairment:** The usual dose of ZESTRIL (10 mg) is recommended for patients with creatinine clearance > 30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≥ 10 mL/min ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 5 mg once daily. For patients with creatinine clearance < 10 mL/min (usually on hemodialysis) the recommended initial dose is 2.5 mg. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Renal Status	Creatinine Clearance mL/min	Initial Dose mg/day
Normal Renal Function to Mild Impairment	>30	10
Moderate to Severe Impairment	≥10 ≤30	5
Dialysis Patients	<10	2.5‡

‡Dosage or dosing interval should be adjusted depending on the blood pressure response.

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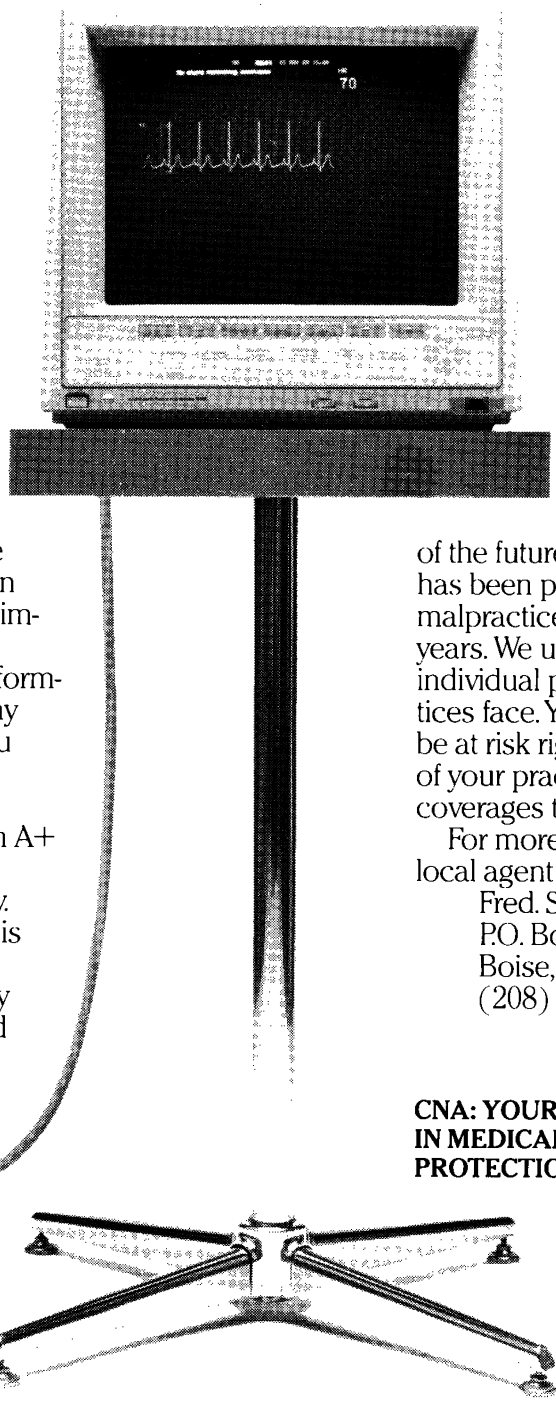

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The following is a brief summary only. Before prescribing, see complete prescribing information in Tenex product labeling.

Contraindications: Tenex is contraindicated in patients with known hypersensitivity to guanfacine hydrochloride.

Precautions: *General.* Like other antihypertensive agents, Tenex (guanfacine hydrochloride) should be used with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease or chronic renal or hepatic failure.

Sedation. Tenex, like other orally active central alpha-2 adrenergic agonists, causes sedation or drowsiness, especially when beginning therapy. These symptoms are dose-related (see Adverse Reactions). When Tenex is used with other centrally active depressants (such as phenothiazines, barbiturates, or benzodiazepines), the potential for additive sedative effects should be considered.

Rebound. Abrupt cessation of therapy with orally active central alpha-2 adrenergic agonists may be associated with increases (from depressed on-therapy levels) in plasma and urinary catecholamines, symptoms of "nervousness and anxiety" and, less commonly, increases in blood pressure to levels significantly greater than those prior to therapy.

Information for Patients. Patients who receive Tenex should be advised to exercise caution when operating dangerous machinery or driving motor vehicles until it is determined that they do not become drowsy or dizzy from the medication. Patients should be warned that their tolerance for alcohol and other CNS depressants may be diminished. Patients should be advised not to discontinue therapy abruptly.

Laboratory Tests. In clinical trials, no clinically relevant laboratory test abnormalities were identified as causally related to drug during short-term treatment with Tenex (guanfacine hydrochloride).

Drug Interactions. No specific adverse drug interactions have been identified, but the potential for increased sedation when Tenex is given with other CNS-depressant drugs should be appreciated.

Anticoagulants. Ten patients who were stabilized on oral anticoagulants were given guanfacine, 1–2 mg day, for 4 weeks. No changes were observed in the degree of anticoagulation.

In several well-controlled studies, guanfacine was administered together with diuretics with no drug interactions reported. In the long-term safety studies, Tenex was given concomitantly with many drugs without evidence of any interactions. The principal drugs given (number of patients in parentheses) were: cardiac glycosides (115), sedatives and hypnotics (103), coronary vasodilators (52), oral hypoglycemics (45), cough and cold preparations (45), NSAIDs (38), antihyperlipidemics (29), antigout drugs (24), oral contraceptives (18), bronchodilators (13), insulin (10), and beta blockers (10).

Drug/Laboratory Test Interactions. No laboratory test abnormalities related to the use of Tenex (guanfacine hydrochloride) have been identified.

Carcinogenesis, Mutagenesis, Impairment of Fertility. No carcinogenic effect was observed in studies of 78 weeks in mice at doses more than 150 times the maximum recommended human dose and 102 weeks in rats at doses more than 100 times the maximum recommended human dose. In a variety of test models guanfacine was not mutagenic.

No adverse effects were observed in fertility studies in male and female rats.

Pregnancy Category B. Administration of guanfacine to rats at 70 times the maximum recommended human dose and rabbits at 20 times the maximum recommended human dose resulted in no evidence of impaired fertility or harm to the fetus. Higher doses (100 and 200 times the maximum recommended human dose in rabbits and rats respectively) were associated with reduced fetal survival and maternal toxicity. Rat experiments have shown that guanfacine crosses the placenta.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery. Tenex (guanfacine hydrochloride) is not recommended in the treatment of acute hypertension associated with toxemia of pregnancy. There is no information available on the effects of guanfacine on the course of labor and delivery.

Nursing Mothers. It is not known whether Tenex (guanfacine hydrochloride) is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Tenex is administered to a nursing woman. Experiments with rats have shown that guanfacine is excreted in the milk.

Pediatric Use. Safety and effectiveness in children under 12 years of age have not been demonstrated. Therefore, the use of Tenex in this age group is not recommended.

Adverse Reactions: Adverse reactions noted with Tenex (guanfacine hydrochloride) are similar to those of other drugs of the central α-2 adrenoreceptor agonist class: dry mouth, sedation (somnolence), weakness (asthenia), dizziness, constipation, and impotence. While the reactions are common, most are mild and tend to disappear on continued dosing.

Skin rash with exfoliation has been reported in a few cases; although clear cause and effect relationships to Tenex could not be established, should a rash occur, Tenex should be discontinued and the patient monitored appropriately.

In a 12-week placebo-controlled, dose-response study the frequency of the most commonly observed adverse reactions showed a clear dose relationship from 0.5 to 3 mg, as follows:

Adverse Reaction	Assigned Treatment Group				
	Placebo	0.5 mg	1.0 mg	2.0 mg	3.0 mg
n =	73	72	72	72	72
Dry Mouth	5 (7%)	4 (5%)	6 (8%)	8 (11%)	20 (28%)
Somnolence	1 (1%)	3 (4%)	0 (0%)	1 (1%)	10 (14%)
Asthenia	0 (0%)	2 (3%)	0 (0%)	2 (2%)	7 (10%)
Dizziness	2 (2%)	1 (1%)	3 (4%)	6 (8%)	3 (4%)
Headache	3 (4%)	4 (3%)	3 (4%)	1 (1%)	2 (2%)
Impotence	1 (1%)	1 (1%)	0 (0%)	1 (1%)	3 (4%)
Constipation	0 (0%)	0 (0%)	0 (0%)	1 (1%)	1 (1%)
Fatigue	3 (3%)	2 (3%)	2 (3%)	5 (6%)	3 (4%)

There were 41 premature terminations because of adverse reactions in this study. The percent of patients who terminated and the dose at which they terminated were as follows:

Dose:	Placebo	0.5 mg	1 mg	2 mg	3 mg
Terminated:	6.9%	4.2%	3.2%	6.9%	8.3%

Reasons for dropouts among patients who received guanfacine were: somnolence, headache, weakness, dry mouth, dizziness, impotence, insomnia, constipation, syncope, urinary incontinence, conjunctivitis, paresthesia, and dermatitis.

In a second placebo-controlled study in which the dose could be adjusted upward to 3 mg per day in 1-mg increments at 3-week intervals, i.e., a setting more similar to ordinary clinical use, the most commonly recorded reactions were: dry mouth 47%, constipation 16%, fatigue 12%, somnolence 10%, asthenia 6%, dizziness 6%, headache 4%, and insomnia 4%.

Reasons for dropouts among patients who received guanfacine were: somnolence, dry mouth, dizziness, impotence, constipation, confusion, depression, and palpitations.

In the clonidine guanfacine comparison described in Clinical Pharmacology, the most common adverse reactions noted were:

	Guanfacine (n = 279)	Clonidine (n = 278)
Dry mouth	30%	37%
Somnolence	21%	35%
Dizziness	11%	8%
Constipation	10%	5%
Fatigue	9%	8%
Headache	4%	4%
Insomnia	4%	3%

Adverse reactions occurring in 3% or less of patients in the three controlled trials were:

Cardiovascular—	bradycardia, palpitations, substernal pain
Gastrointestinal—	abdominal pain, diarrhea, dyspepsia, dysphagia, nausea
CNS—	amnesia, confusion, depression, insomnia, libido decrease
ENT disorders—	rhinitis, taste perversion, tinnitus
Eye disorders—	conjunctivitis, iritis, vision disturbance
Musculoskeletal—	leg cramps, hypokinesia
Respiratory—	dyspnea
Dermatologic—	dermatitis, pruritus, purpura, sweating
Urogenital—	testicular disorder, urinary incontinence
Other—	malaise, paresthesia, paresis

Adverse reaction reports tend to decrease over time. In an open-label trial of one year's duration, 580 hypertensive subjects were given guanfacine, titrated to achieve goal blood pressure, alone (51%), with diuretic (38%), with beta blocker (3%), with diuretic plus beta blocker (6%), or with diuretic plus vasodilator (2%). The mean daily dose of guanfacine reached was 4.7 mg.

Adverse Reaction	Incidence of adverse reactions at any time during the study	Incidence of adverse reactions at end of one year
N	580	580
Dry mouth	60%	15%
Drowsiness	33%	6%
Dizziness	15%	1%
Constipation	14%	3%
Weakness	5%	1%
Headache	4%	0.2%
Insomnia	5%	0%

There were 52 (8.9%) dropouts due to adverse effects in this 1-year trial. The causes were: dry mouth (n = 20), weakness (n = 12), constipation (n = 7), somnolence (n = 3), nausea (n = 3), orthostatic hypotension (n = 2), insomnia (n = 1), rash (n = 1), nightmares (n = 1), headache (n = 1), and depression (n = 1).

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Deadline: Nominations must be received by

December 1, 1989

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March 2 through 7, 1990
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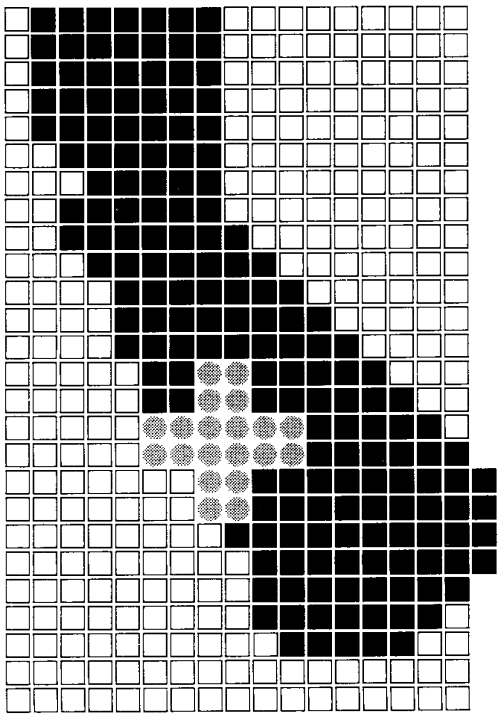
ANNUAL SESSION



Western Scientific Assembly offers over 30 CME Programs for physicians of all specialties, with topics that include sports medicine, HIV infection, asthma, cocaine, reproductive hazards, skin cancer, and difficult wound care.

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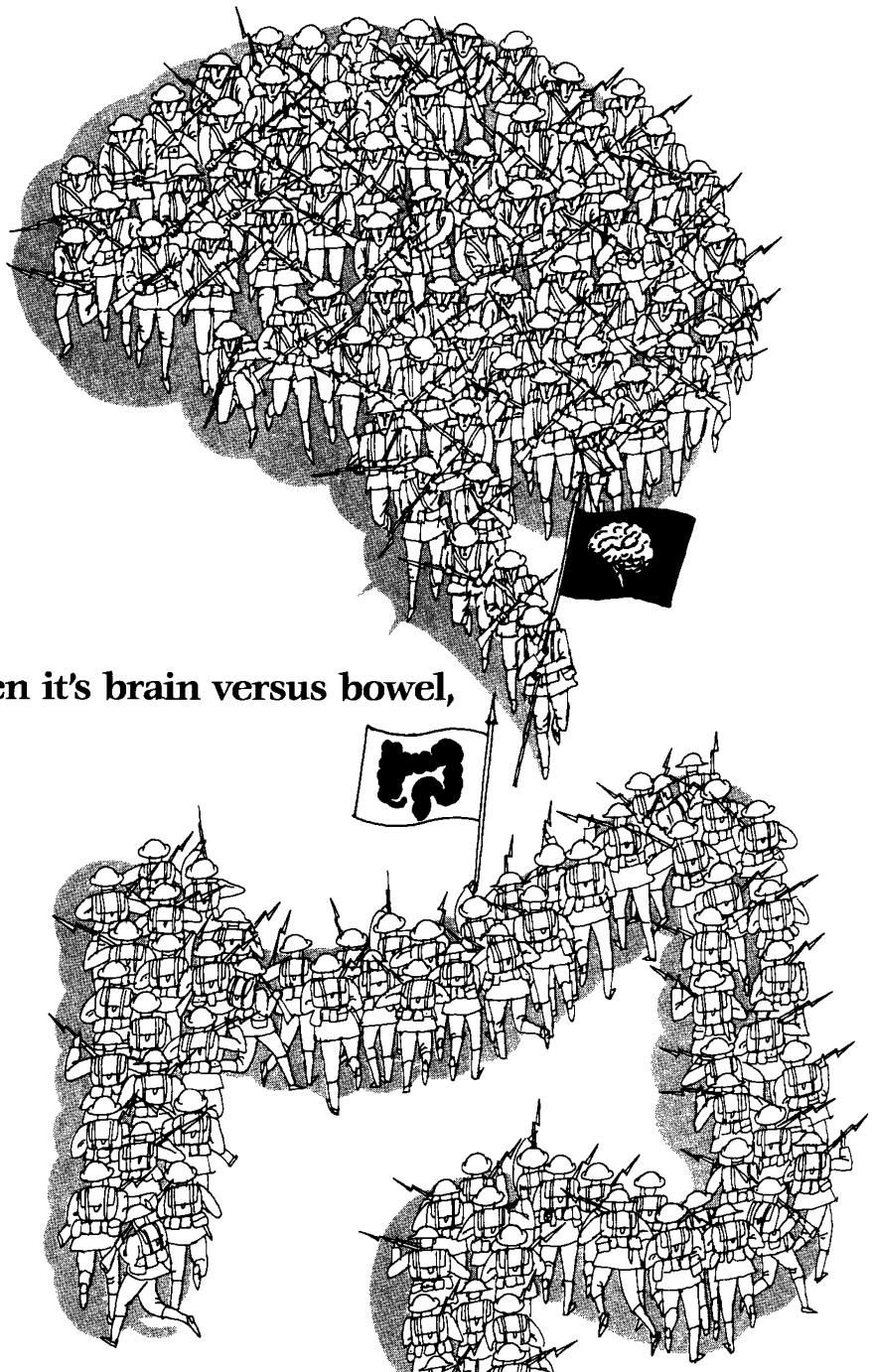

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BC/BE INTERNIST being sought to establish practice in resort community of Ruidoso, New Mexico. Beautiful mountain setting with easy access to all forms of recreation. Financial assistance may be available for the right individual. For more details, please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

FAMILY PRACTITIONER, JUNEAU, ALASKA. Busy three physician Family Practice group (including OB) seeks replacement for partner departing fall 1989. Located in Alaska's capital city in the Tongass National Forest, offering year 'round recreation including skiing, boating, and hiking. Guaranteed salary with excellent fringe benefits and opportunity for partnership within one year. Send CV to Sarah A. Isto, MD, Valley Medical Care, Inc, 9309 Glacier Hwy, B-301, Juneau, AK 99801; (907) 789-3181.

OB/GYN, INTERNISTS, Family Practitioners, Pediatricians for Arizona and western opportunities. Quality positions available other regions of country. Inquiries confidential. Mitchell & Associates, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080.

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BC/BE INTERNIST being recruited for the community of Artesia, New Mexico. Solo practice with cross-coverage available from local Internist. Community-based financial assistance may be available for the right individual. Family oriented community with year round recreation; excellent weather. Fully equipped 38-bed hospital. For more information, please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

(Continued on Page 582)

(Continued from Page 581)

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BC/BE FAMILY PRACTICE opportunity in Tucumcari, New Mexico. Must be willing to do OB. Financial assistance with income guarantee. For more information, please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

BC/BE FAMILY PRACTITIONER sought to join an established practice in the community of Artesia, New Mexico. Income guarantee available for the right individual. Family oriented community with year round recreation and fully equipped 38-bed hospital. Please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

BC/BE FAMILY PRACTITIONER sought for small community on the western slopes of the Rocky Mountains. Income guarantee available for the right individual. For more information on this opportunity, please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

BC/BE FAMILY PRACTICE opportunity in the resort community of Ruidoso, New Mexico. Financial assistance with income guarantee. Beautiful mountain setting with easy access to all forms of recreation. For further details, please send your résumé to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

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MD TO ASSIST in busy Orthopedic clinic and Operating Room. Will also take call. Position has been used in the past as a bridge to orthopedic residency. Attractive salary and excellent benefit package. Washington State licensure required. Available immediately. Send CV or contact Mary Anderson, Personnel Representative, Pacific Medical Center, 1200-12th Ave S., Seattle, WA 98144; (206) 326-4111.

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HEALTH OFFICER

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(Continued on Page 584)

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It's not just different in the Army Reserve, there are opportunities to explore other phases of medicine, to add knowledge, and to develop important administrative skills. There are enough different needs to fill right in your local Army Reserve unit to make a weekend a month exciting and rewarding.

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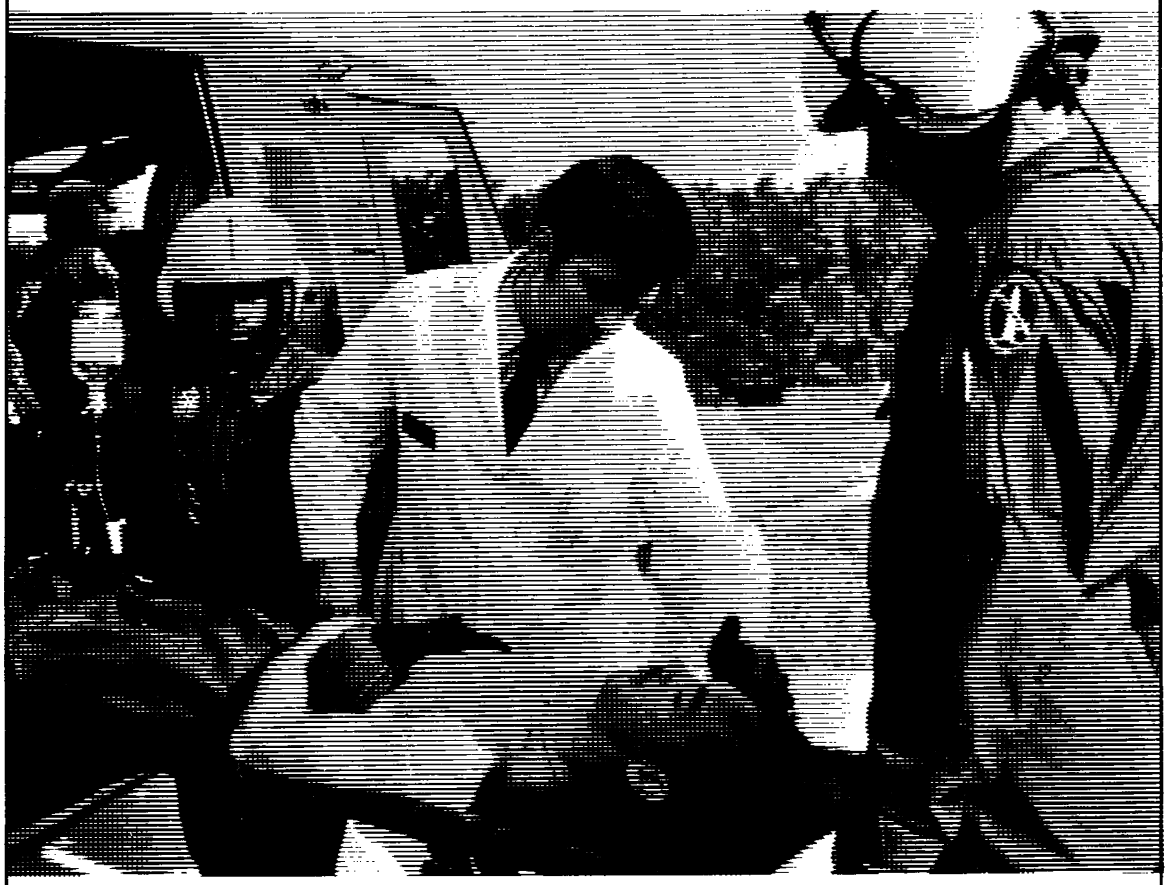

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(Continued from Page 582)

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Several positions available for Family Practice, Internal Medicine, and most medical subspecialties. We are a young, aggressive group in a well known prepaid group practice HMO organization with excellent benefits and a very reasonable call schedule. You will have a rewarding practice opportunity with ample time to enjoy the mountains and San Francisco which are nearby. If interested please call or send CV to Physician Recruitment, Administration, The Permanente Medical Group, Inc, 1305 Tommydon St, Stockton, CA 95210; (209) 476-3300.

SAN DIEGO. Well established, multispecialty group composed of Family Physicians, General Internists, OB/GYNs, Pediatricians, General Surgeons, ENT, and Ophthalmologist is expanding. Those interested in joining a vital private practice group, with emphasis in primary care and seeing fee-for-service and managed care patients, are welcome to send CV to Miriam Stephens Drake, 1450 Frazee Rd, Ste 605-1, San Diego, CA 92018; (619) 295-0599.

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For all specialties for hospitals, clinics, multispecialty groups, partnership and solos. Contact Jim Grant in complete confidence at the bay area specialists, **Len Nugent and Co, 1400 Coleman, Ste B-22, Santa Clara, CA 95050; or call (408) 727-2478, FAX # (408) 727-7390.** Never a fee to the physician.

AMBULATORY CARE. Join our partnership of established Emergency and Ambulatory Care Physicians. Part-time, full-time, and directorship positions available. Malpractice paid, competitive salary, growth opportunity. Prefer BC/BE in appropriate primary care specialties. If you're interested in a secure, rewarding career position, contact Jane Dressler, California Emergency Physicians, 2101 Webster St, Ste 1050, Oakland, CA 94612-3027.

PUGET SOUND. BC/BE Family Practitioner for new branch office of multispecialty clinic. Full Family Practice opportunity, OB optional. Guaranteed starting salary and benefits. Respond with CV to Memorial Clinic, Attention: Inge Hart, Personnel, 500 N. Lilly Rd, Olympia, WA 98506; (206) 456-1122, ext 249.

INTERNIST. Live in San Francisco and commute to nearby rural area for four two-night shifts per month in combined Internal Medicine/Emergency Room practice. Five Internists currently working in stable group. Practice quality medicine in the country where you can make a greater impact and enjoy lots of free time wherever you like to live. $72k per year. Charles Rath, MD, 199 E. Webster St, Colusa, CA 95932; (916) 458-7739.

GYNECOLOGIST needed for 78-bed JCAHO hospital. We are growing and we need to enlarge our specialty staff. Just opened new Cancer Treatment Center. 12,000 community, 90,000 immediate service area, 160,000 catchment area. Great outdoors area, cattle, oil, gas, hunting, fishing, good schools, low crime, ideal area for raising children. Reasonable malpractice rates. Send CV to Marilyn Bryan, Community Hospital, PO Box 2339, Elk City, OK 73648; (405) 225-2511.

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To inquire, write:

Director of Medical Staff Personnel
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Seattle, WA 98121

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- Three to five years clinical experience in a managed care setting
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Send résumé/CV to:

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Huntington Beach, CA 92647

SAN FRANCISCO BAY AREA. BE/BC Internist. We currently are seeking highly qualified Internists and subspecialists to complement our energetic Internal Medicine team. Department members provide a full range of medical services for a population of over 200,000 prepaid Health Plan members. Recently renovated and expanded medical center facilities are within convenient commuting distance to virtually any bay area city and the extensive cultural and recreational activities of northern California. As part of our large, multispecialty group practice, you would enjoy an excellent salary, generous fringe benefits, a flexible schedule, and the opportunity for academic affiliation with prestigious local institutions. Send CV to Michael Getzell, MD, Chief, Dept of Internal Medicine, Kaiser Permanente Medical Center, 27400 Hesperian Blvd, Hayward, CA 94545.

SAN FRANCISCO AREA. Family Practitioner or Primary Care Internist to join progressive six physician group in lovely coastside community of Half Moon Bay, 25 miles south of San Francisco. CV to Dr Larry Casalino, 225 S. Cabrillo Hwy, Half Moon Bay, CA 94019.

MULTIPLE FAMILY PRACTICE (BC/BE) positions available in several suburban satellite clinics of a large Seattle area multispecialty group practice. Diverse patient population includes managed care, fee-for-service, and retired military (at some satellite clinics). Competitive salary and excellent benefits. Contact Mary Anderson, Pacific Medical Center, 1200 12th Ave S., Seattle, WA 98144; (206) 326-4111.

SAN FRANCISCO. Outstanding opportunity for BC/BE Internist or Family Practitioner at 260-bed community hospital in the rapidly growing South of Market area. Excellent opportunity to build or join busy practices. Competitive salary and benefits package. Send CV to Walter Kopp, St Luke's Hospital, 3555 Army St, San Francisco, CA 94110; (415) 641-6543.

COLORADO, WASHINGTON, NORTHERN CALIFORNIA. Exceptional practice opportunities now available in Family Practice, Pediatrics, Internal Medicine, Psychiatry, and OB. Send CV to D. A. Franklin, MD, and Associates, 4894 Sterling Dr, Boulder, CO 80301.

(Continued on Page 585)

(Continued from Page 584)

PHYSICIANS WANTED

POSITIONS AVAILABLE
For BC/BE physicians in California and nationwide in the following specialties: ENT, Family, Internal, Neurology, Neurosurgery, OB/GYN, Ophthalmology, Orthopedics, Pediatrics, Urgent Care. Excellent salary/benefits. Private practices also for sale in northern California. Send CV or call **BRADSHAW ASSOCIATES, 21 Altamount Dr, Orinda, CA 94563; (415) 376-0762.**

CALIFORNIA. BC/BE OTOLARYNGOLOGIST to join 14 MD multispecialty group with progressive practice environment located in a small city in the central San Joaquin Valley at the foothills of the Sierras, two hours from the coast. Send CV to Kaweah Medical Group, Attn: Maya Ricci, 222 W. Willow, Visalia, CA 93291.

FAMILY PRACTITIONER, BC/BE for community health center. Excellent opportunity in the culturally rich Four-Corners area of northwest New Mexico. Near 110-bed hospital, four physicians with mid-levels in integrated system of health and human services. Outstanding benefit package. Recreational paradise in community of 30,000. Contact Sheila Brenner, Farmington Community Health Center, PO Box 3239, Farmington, NM 87499; (505) 327-4796.

MEDICAL ONCOLOGIST BC/BE to join expanding 32 physician multispecialty group practice located in the foothills of the Blue Mountains in the state of Washington. The clinic serves a population area of 150,000. Full range of Radiation Oncology services are available in the community. Excellent schools, cultural and recreational opportunities. One junior college and two four-year colleges are located in the community. Guaranteed income with excellent benefit program. Send CV to Connie Goude, Walla Walla Clinic, 55 W. Tietan, Walla Walla, WA 99362.

GENERAL SURGEON BC/BE sought to join busy, moderate-sized, multispecialty group practice. Located 25 miles south of San Francisco, adjacent to 400-bed state-of-the-art hospital. Unsurpassed climate and life-style near city, ocean, and mountain pursuits. Quality educational and employment opportunities for children and spouse. Excellent salary, vacation, and benefits commensurate with experience. Early partnership. Send CV to Number 171, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

ORTHOPEDIC SURGEON BC/BE sought to join two physician department in busy, moderate-sized, multispecialty group practice. Located 25 miles south of San Francisco, adjacent to 400-bed state-of-the-art hospital. Unsurpassed climate and life-style near city, ocean, and mountain pursuits. Quality educational and employment opportunities for children and spouse. Excellent salary, vacation, and benefits commensurate with experience. Early partnership. Send CV to Number 171, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

UROLOGIST, southern California. Urology group seeking new highly qualified BC partner. Ability in all radical surgery, ESWL, Endourology, prostheses, etc desired. Excellent smog-free coastal locale. Busy, expandable practice. Send CV to Number 157, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

ONCOLOGIST NEEDED for multispecialty group practice in Seattle; affiliated with University of Washington. Full-time clinical with potential for research. Diverse patient population includes managed care, fee-for-service, retired and active duty military. Attractive salary plus incentive and excellent benefit package. Send CV or contact Mary Anderson, Personnel Representative, Pacific Medical Center, 1200 12th Ave S., Seattle, WA 98144; (206) 326-4111.

(Continued on Page 586)

NORTHERN CALIFORNIA

The Permanente Medical Group, a growing multispecialty group, is recruiting physicians in a variety of specialties for positions throughout our beautiful Northern California region: the San Francisco Bay Area, Sacramento and the Central Valley.

MARTINEZ

Emergency Physicians — Join friendly, relaxed and highly professional colleagues at our 204-bed hospital in the heart of the San Francisco Bay Area. We are seeking experienced physicians, BE/BC preferred. Locum Tenens and part-time work available Summer/Fall, 1989 & Winter/Spring, 1990. Recent adjustments provide excellent hourly rate plus paid malpractice. Career positions also available, providing salary and excellent benefits package. Send CV to: Ted Bayer, M.D., Chief, or Andrea Wagner, M.D., Asst. Chief, Department of Emergency Services, The Permanente Medical Group, Inc., 200 Muir Road, Martinez, CA 94553. (415) 372-1000, ext. 3316 or (415) 372-1124.

Internists and Cardiologist (BC/BE) - Join us in our high quality, expanding, 25 member Department of Medicine where you will benefit from our university affiliated internal medicine residency program. Faculty appointment available. This East Bay suburban setting has excellent schools, and is only 25 miles from San Francisco. Please send CV, or contact Michael Melewicz, M.D., Dept. of Medicine, The Permanente Medical Group, Inc., 200 Muir Road, Martinez, CA 94553. (415) 372-1069.

ROSEVILLE

General Internists (BC/BE) — Immediate openings for California licensed Internists at our Roseville facility, 90 miles from San Francisco or Sierra skiing & camping. University associated residency program. Send CV to: Tony Cantelmi, M.D., The Permanente Medical Group, Inc., 1001 Riverside Blvd., Roseville, CA 95678.

SAN JOSE

Family Practitioner (BC/BE) — Our 228-bed Santa Teresa Medical Center serves 128,000 members. Predominately outpatient practice located in Silicon Valley, approximately 45 minutes south of San Francisco and 30 minutes from the Pacific Coast. Send CV to D. Bardole, The Permanente Medical Group, Inc., 260 International Circle, San Jose, CA 95119.

Surgeons (BC/BE) - One General Surgeon and one Surgeon to do both general and vascular surgery. We are a 9 surgeon department with modern offices adjacent to the 228-bed hospital equipped with 7 operating rooms. We handle a full range of general, thoracic, vascular and plastic surgery cases, and our group includes about 100 fully trained physicians in all specialties. Please apply to the Oakland address below.

SOUTH SAN FRANCISCO

Seeking highly-motivated **BC/BE Internists and a BC/BE Gastroenterologist-Internist** for this expanding practice adjacent to our 125-bed community hospital. Send CV to: Mark Cole, M.D., Dept. of Medicine, The Permanente Medical Group, Inc., 1200 El Camino Real, So. San Francisco, CA 94080.

FAIRFIELD

Excellent opportunity for **BC/BE Family Practitioner** to join a growing department. Multispecialty clinic emphasizing personalized care. Full hospital privileges including ICU/CCU, but no Obstetrics. Very favorable call schedule. Forward CV to: Steven Freedman, M.D., The Permanente Medical Group, Inc., 1550 Gateway Blvd., Fairfield, CA 94533. (707) 427-4260.

Members of our large, multispecialty group earn a highly competitive salary and excellent benefits including scheduled time off, malpractice insurance, medical, dental and life insurance, and a substantial retirement program. Our physicians are free to concentrate on providing quality health care, without the burdens of managing a practice.

To inquire about other openings with our successful, growing medical group, send CV to: Richmond Prescott, M.D., Physician Recruitment Services, Dept. WJM-5114, The Permanente Medical Group, Inc., 1814 Franklin, 4th Floor, Oakland, CA 94612. (415) 987-4949. EOE

KAISER PERMANENTE
Good People. Good Medicine.

(Continued from Page 585)

PHYSICIANS WANTED

PHYSICIANS/ SURGEONS

Practice opportunities available now in these and other medical/surgical specialties:

FAMILY PRACTITIONER

Live and work in rural areas of Kansas or North Dakota. Generous compensation packages.

ANESTHESIOLOGIST

Clinical/academic position with prestigious Children's Hospital in Southern U.S. for BC Pediatric Anesthesiologist.

GENERAL SURGEON

Women's health center at Central California hospital seeks BC general surgeon. Must support concept of women treating women.

For immediate consideration for these and other opportunities, call collect or send current CV:

HURD/CAMPBELL

Department TWJM
100 East Wardlow Road, Suite 100
Long Beach, California 90807
Telephone (213) 595-1101

SOUTHERN CALIFORNIA

Specialists and Primary Care Physicians—CIGNA Healthplans invites you to join our innovative and dynamic managed health care team. Our multidisciplinary HMO practice provides a supportive and collegial work environment at 31 locations. You will enjoy a wealth of cultural and recreational activities, access to major academic centers, and an excellent compensation package. *Call collect* **(818) 500-6570** *or send CV to* **Robert Harrington, MD, Professional Recruitment, CIGNA Healthplans of California, 505 N. Brand Blvd, Ste 400-49, Glendale, CA 91203.**

PEDIATRICIAN BC/BE sought to join four physician department in busy, moderate-sized, multispecialty group practice. Located 25 miles south of San Francisco, adjacent to 400-bed state-of-the-art hospital. Unsurpassed climate and life-style near city, ocean, and mountain pursuits. Quality educational and employment opportunities for children and spouse. Excellent salary, vacation, and benefits commensurate with experience. Early partnership. Send CV to Number 171, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

OBSTETRICIAN/GYNECOLOGIST BC/BE sought to join three physician department in busy, moderate-sized, multispecialty group practice. Located 25 miles south of San Francisco, adjacent to 400-bed state-of-the-art hospital. Unsurpassed climate and life-style near city, ocean, and mountain pursuits. Quality educational and employment opportunities for children and spouse. Excellent salary, vacation, and benefits commensurate with experience. Early partnership. Send CV to Number 171, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

CENTRAL CALIFORNIA. Join our team of Family Practice Physicians in a community health clinic setting near Fresno, California. We offer a contract arrangement with competitive salaries and benefits, malpractice paid. We are affiliated with the UC San Francisco teaching program. Central California has Yosemite National Park, excellent family recreation, low housing costs, with both urban and rural life-styles. Contact Dr Donn Cobb, Health Officer, Fresno County Dept of Health, PO Box 11867, Fresno, CA 93775; (209) 445-3202.

PHYSICIANS WANTED

EMERGENCY MEDICINE OPPORTUNITIES

OREGON • NEVADA • WASHINGTON

Emergency department opportunities, including directorship, are available with Spectrum Emergency Care at the following client hospitals:

Astoria, Oregon: Located on the Oregon coast. Moderate volume ED. Annual reimbursement $80,000 +.

Tillamook, Oregon: Located on the Oregon coast. Moderate volume ED. Annual reimbursement $69,000 +.

Fallon, Nevada: One hour from Reno. Low volume ED. Annual reimbursement $73,000 +.

Boulder City, Nevada: Half hour from Las Vegas. Low volume ED. Annual reimbursement $69,000 +.

Elko, Nevada: Located in central Nevada. Moderate volume ED. Annual reimbursement exceeds $80,000.

Yakima, Washington: Director and staff positions at Osteopathic hospital. Low volume ED/urgent care setting. Annual reimbursement $69,000 +.

As an independent contract physician with Spectrum, you are offered:

- High-limit occurrence malpractice insurance
- Allowance for CME, professional dues, licensure fees, and relocation expenses
- Directors offered annual administrative stipend and health benefits

Call 1-800-288-8044 for details.

ARA services

SPECTRUM EMERGENCY CARE, Inc.

John Brown

1155 Kelly Johnson Blvd., Suite 305 Colorado Springs, CO 80920

CALIFORNIA MULTISPECIALTY. Cardiologist, Anesthesiologist, Infectious Disease Specialist, Internal Medicine, Pediatrician, Endocrinologist, Orthopedist, General/Family Practitioner, Obstetrician/Gynecologist, Pathologist, General/Thoracic Surgeon. Excellent opportunity for physicians in Los Angeles suburb to join 100 member multispecialty medical group. Large fee-for-service and prepaid practice, no Medi-Cal. Excellent compensation program based on guarantee plus incentive, profit sharing and pension plan. Group provides health, dental, life, and malpractice. Partnership in real estate and medical corporation available. Send CV to Ron McDaniel, Assistant Administrator, Mullikin Medical Center, 17821 S. Pioneer Blvd, Artesia, CA 90701.

HAWAII. Family Practitioner needed for rural underserved area. Full-time position in nonprofit community health clinic. No OB, hospitalizations optional. Desire dedicated person to work in multicultural setting. Contact Alan Chun, MD, Waianae Coast Comprehensive Health Center, 86-260 Farrington Hwy, Waianae, HI 96792; (808) 696-7081.

BC/BE NEUROLOGIST to join progressive San Francisco bay area HMO. Busy clinical practice in desirable Marin County. Competitive income and excellent benefits. Please contact Jonathan Freudman, MD, Assistant Chief, Dept of Internal Medicine, The Permanente Medical Group, Inc, 99 Montecillo Rd, San Rafael, CA 94903. AA/EOE employer.

ENDOCRINOLOGIST NEEDED to join a busy solo Endocrinologist in a growing southern California city. Established referral base, 300-bed acute care hospital. Competitive salary leading to partnership. Reply with CV to Number 169, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

MARICOPA COMMUNITY MEDICINE ASSOCIATES of Phoenix, Arizona, is staffing 60 plus physicians, physician assistants, and nurse practitioners for Maricopa County's ambulatory care clinics at various locations in the Phoenix metropolitan area. General Practice, Family Practice, and Internal Medicine specialist openings. Maricopa Medical Center, Dept of Community Medicine, 4th Floor, 2601 E. Roosevelt, Phoenix, AZ 85008; (602) 267-5288.

SAN JUAN ISLANDS, WASHINGTON. Established, well-equipped 8,500 square foot community-owned clinic with complete emergency facilities seeks two BC/BE ACLS certified Family Physicians. Immediate employment, competitive salaries and benefits. Adjacent 85-bed nursing home. Superb scenic and recreational area. Send résumé to Leonard Eliel, MD, Box 370, Friday Harbor, WA 98250. An EO Employer.

EUGENE CLINIC, EUGENE, OREGON

Dynamic 55 physician multispecialty group with seven locations seeks BC/BE physicians in the following specialties: Dermatology, Family Practice, Geriatrics, Infectious Diseases, Internal Medicine, OB/GYN, Occupational Medicine, Orthopedics, General Surgery (breast disease focus), Urology. Eugene, attractive university town within 60 mile radius of Cascade Mountains and Oregon coast, offers superlative life-style, fine school system, active and varied cultural opportunities, and unlimited recreation. Qualified candidates send CV and three letters of reference to:

Physician Recruiter
1162 Willamette St
Eugene, OR 97401

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PHYSICIANS WANTED

NORTHERN CALIFORNIA. Rapidly expanding HMO in the San Francisco bay area is currently seeking three highly motivated BE/BC Family Practice/Emergency Room Physicians for the Urgent Care Center in a career and/or temporary position. Our 228-bed community hospital offers excellent specialty support, flexible hours, and competitive salaries. Career physicians are offered many benefits including malpractice insurance, medical, dental, and group life insurance, vacation, sick and educational leave, excellent retirement benefits, and special arrangements for physicians transferring from established practice. For more information, please send CV or contact Edward Cheng, MD, Dept of Urgent Care, The Permanente Medical Group, Inc, 260 International Circle, San Jose, CA 95119-1197; (408) 972-6110. EOE.

INTERNIST BC/BE needed to join busy pulmonary subspecialty practice in rapidly expanding area near Seattle, Washington. Affiliated with 200 plus-bed and expanding hospital. Other subspecialty welcome, but not necessary. Excellent salary with incentive, benefits, office space, and practice support. Send CV and references to Business Manager, Eastside Pulmonary Associates, 1603-116th Ave NE, Ste #112, Bellevue, WA 98004.

TUCSON, ARIZONA. BC/BE, residency trained Family Physician sought to join busy solo Family Physician in private practice. Attractive start-up package available. Send CV to Herb Jalowsky, MD, 1701 W. St Mary's Rd, Tucson, AZ 85745; (602) 622-1414.

PHOENIX, ARIZONA. Maricopa County, Department of Corrections is seeking Internists, General and Family Practitioners, and Certified Physician Assistants. Prefer experience in adult ambulatory care. Five weeks paid vacation, ten holidays, one week CME. Excellent hours—minimal on call. Paid malpractice. Paid health insurance. Facilities include both infirmary and family practice clinic settings providing a good working atmosphere. Send CV to Maricopa Medical Center, Dept of Community Medicine, 2601 E. Roosevelt, Phoenix, AZ 85008; (602) 267-5288.

CARDIOLOGY. Cardiologist BC/BE to join two other Cardiologists in eight physician multispecialty clinic in Seattle. Extensive invasive/noninvasive opportunities. Send CV to PO Box 364, Seahurst, WA 98062.

CALIFORNIA
FAMILY PRACTICE

Established medical group seeks a BC/BE eligible Family Practice physician to join them in private practice.

Physician would assist in providing full spectrum of Family Practice care, including obstetrics. Competitive salary and benefit program, as well as an opportunity for a partnership in the practice. Send your CV to the attention of:

Cindy Holston,
1237 Rose Avenue,
Selma, CA, 93662
or phone **209/896-6370**

We are located in Central California, where housing costs are reasonable and recreational activities are numerous.

PHYSICIANS WANTED

WASHINGTON STATE
ROCKWOOD CLINIC, PS

An expanding 65 physician multispecialty fee-for-service group seeks BC/BE physicians in the following specialties:

ALLERGY	HEMATOLOGY/ONCOLOGY
CARDIOLOGY	OB/GYN
DERMATOLOGY	RHEUMATOLOGY
INTERNAL MEDICINE	GENERAL SURGERY

FAMILY PRACTICE—permanent, part-time, locum tenens

Attractive benefit package includes competitive salary leading to early shareholder status.

CONTACT: **Colleen Mooney, Recruitment Coordinator**
Rockwood Clinic, PS
E. 400 Fifth Ave
Spokane, WA 99202
(509) 838-2531

COME ENJOY SPOKANE'S QUALITY LIFE-STYLE!

UNIVERSITY PHYSICIANS. Student Health Service, University of Wyoming, Laramie, is seeking physicians for full-time employment. Applicants must have a Medical Doctor's degree plus be BC/BE by either AAFP or American Board of Internal Medicine. Must have a license or qualify for licensure to practice medicine in the state of Wyoming. Prefer candidate to have at least four years of primary care experience. Physicians to join two full-time physicians to care for 10,000 students on the campus at Laramie, Wyoming. The Student Health Service has its own laboratory, x-ray, and pharmacy. Salary commensurate with qualifications and experience. Closing date: October 25, 1989, or until positions are filled. Send inquiries and/or CV to Albert H. Roth, MD, Acting Director, Student Health Service, University of Wyoming, PO Box 3068, Laramie, Wyoming 82071. EOE/AA.

ENDOCRINOLOGIST. Outstanding opportunity for a BC/BE Endocrinologist to join busy hospital-based group in Berkeley. Send CV to Randall Ammon, MD, Endocrinology Dept, 3001 Colby St, Berkeley, CA 94705.

ACADEMIC INTERNIST—Los Angeles area—general or subspecialty. Primarily inpatient teaching—Family Practice residents. Full-time. Director, Northridge Hospital Family Practice Residency, 18406 Roscoe Blvd, Northridge, CA 91325.

SANTA BARBARA COUNTY FAMILY PRACTICE

California BC/BE Family Practice Physicians sought by Santa Barbara County Health Department for ambulatory practice in Santa Barbara County. Progressive, up to date, and well supported clinical system. Highly qualified physicians will have two to four years experience in county and/or community based outpatient clinics. Fluency in Spanish is highly desirable. Competitive salary DOE. For more information please send current CV to **Elliot Schulman, MD, Santa Barbara County Health Care Services, 300 N. San Antonio Rd, Santa Barbara, CA 93110; (805) 681-5460.** AA/EOE.

FAMILY PRACTICE. The Kaiser Permanente Medical Group's northern California facility in Napa is seeking a BC/BE Family Practitioner to fulfill general clinic and hospital duties. Members of our large, multispecialty group earn highly competitive compensation and outstanding benefits including malpractice insurance, medical, dental, and group life insurance, vacation, educational leave, an excellent retirement program, and special arrangements for physicians transferring from established practice. For more information, please send CV to B. Parmeter, MD, The Permanente Medical Group, 3284 Jefferson St, Napa, CA 94558. EOE.

NORTHERN CALIFORNIA—San Francisco bay area. Leading HMO is seeking BC/BE physician to staff a busy, urban, full-service Emergency Department with the possibility of administrative advancement. Kaiser Permanente is a large prepaid HMO offering competitive salary, job security, shareholder status, and generous benefits including health care, life insurance, disability insurance, sick leave, mortgage assistance, and educational leave. Please address all inquiries to David Witt, MD, Emergency Dept, Kaiser Permanente Medical Center, 1200 El Camino Real, South San Francisco, CA 94080-3299, or call (415) 742-2516. EOE.

SAN FRANCISCO NORTH BAY AREA/NAPA VALLEY. Immediate openings (career and part-time) in a multidiscipline Emergency Department for physicians trained in Emergency Medicine, Internal Medicine, Family Practice, or Pediatrics. Full in-house multispecialty coverage. Complete generous benefit package. Contact Robert Mack, MD, Kaiser Hospital, 975 Sereno Dr, Vallejo, CA 94589; (707) 648-6200. EOE.

Western States OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 300 positions of various specialties. Both permanent and locum tenens. Send CV to:
Western States Physician Services,
5414 E. Montecito, Fresno, CA 93727.
Or call (209) 252-3047.

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PHYSICIANS WANTED

FAMILY PRACTICE

CALIFORNIA

Family Practice physicians needed in a progressive community health center located in Central California. Competitive salary with extra on-call and overtime. Malpractice paid. Generous vacation and time-off policy. Moving and temporary housing allowance to be negotiated. Affiliated with University of California, San Francisco residency program. Position is 60% clinical, 40% teaching. Central California has excellent family recreation, low housing costs, with both urban and rural lifestyles. Send your CV to:

Dr. Donn Cobb, Health Officer
Fresno County Department of Health
P.O. Box 11867
Fresno, CA 93775
209/445-3202

EMERGENCY MEDICINE UNIVERSITY POSITION. The University of California, Davis, School of Medicine, is recruiting for a full-time faculty. The position will be at the Assistant or Associate Professor level. The Division of Emergency Medicine and Clinical Toxicology is undergoing rapid academic development and is applying to have an approved residency program in Emergency Medicine. The UCDMC Emergency Department provides comprehensive emergency service and is a major trauma center in northern California. The Department is a paramedic base station and training center and, in addition, has an active helicopter service and regional poison center. Candidates must be BC/BE in Emergency Medicine and be eligible for licensure in California. A letter outlining teaching background, interests, experience, and research in addition to a CV and the names of five references should be sent to Robert W. Derlet, MD, Chair, Emergency Medicine Search Committee, Tr. 1219, University of California, Davis, Medical Center, 2315 Stockton Blvd, Sacramento, CA 95817. Applications will not be accepted after December 31, 1989. The University of California is an Affirmative Action/Equal Opportunity Employer.

INTERNIST BC/BE. Progressive San Francisco bay area HMO has a full-time Internal Medicine position and a part-time Urgent Care position available. Busy clinical practice with facilities in San Rafael and Petaluma. Competitive income and excellent benefits. Please contact Jonathan Freudman, MD, Assistant Chief, Dept of Internal Medicine, The Permanente Medical Group, Inc, 99 Montecillo Rd, San Rafael, CA 94903. AA/EOE employer.

CALIFORNIA, NORTHERN. A stable group of four ABEM certified/eligible MDs at coastal hospital of 24,000 patient visits would like two new associates. Income $60-$75 per hour. Will consider Family Practice but prefer Emergency Department trained Emergency Physician. Coastal paradise near redwood national parks, minutes from Klammath, Rogue, and Smith Rivers. Video tape of area available. Send CV to EPMG, 120 Montgomery St, Ste 1000, San Francisco, CA 94104.

PHYSICIANS WANTED

NORTH CENTRAL IDAHO

17 physician multispecialty group recruiting BC/BE partners.

- 2nd Dermatologist
- 2nd Gastroenterologist
- 3rd General Internist
- 6th Pediatrician

Progressive medical community. Outstanding recreational area. Excellent life-style.
Send CV to:

Bob Baker, Administrator
Valley Medical Center and Children's Clinic
2318 Vineyard Ave
Lewiston, ID 83501
(208) 746-1383

CARDIOLOGIST—NONINVASIVE/INVASIVE to join four member busy cardiology practice in small town, one hour from Los Angeles. Full range of noninvasive cardiology and active Catheter lab. Position available immediately through July 1990. Send CV to Number 175, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

ONCOLOGY/HEMATOLOGY. Excellent opportunity for Hematologist/Oncologist to join busy Hematology/Oncology practice in central California. Work as little or as much as you want. Excellent salary and opportunity for partnership. Reply to Number 174, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PULMONOLOGIST BC/BE (INTERNAL MEDICINE) with skills in bronchoscopy and management of critically ill patients sought to join busy, moderate-sized, multispecialty group practice. Located 25 miles south of San Francisco, adjacent to 400-bed state-of-the-art hospital. Unsurpassed climate and life-style near city, ocean, and mountain pursuits. Quality educational and employment opportunities for children and spouse. Excellent salary, vacation, and benefits commensurate with experience. Early partnership. Send CV to Number 171, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

CENTRAL CALIFORNIA (FAMILY PRACTICE). We have an opening for a Family Practice Physician. Clinic is a 17,000 square foot primary care facility located near Bakersfield offering medical, dental, lab, x-ray, and pharmacy services. Excellent salary and benefit package. Call George Johnston, (805) 845-3731, for details or write PO Box 457, Lamont, CA 93241.

WANTED: CLINICIAN/TEACHER to join 14 General Internists at Santa Clara Valley Medical Center and Clinics, a public hospital affiliated with Stanford University. Applicants should be BE (BC if eligible more than two years), love clinical medicine and patient care, enjoy housestaff and medical students, and have excellent sense of humor to deal with usual politics of university-affiliated public hospital/clinic work. Send inquiries, CV to Kent Imai, MD, Chief, Primary Care Division, Dept of Medicine, Santa Clara Valley Medical Center, 750 S. Bascom Ave, San Jose, CA 95128.

PSYCHIATRIST, Northern Arizona University. Progressive, accredited student health center is seeking a Psychiatrist to initiate mental health program. Northern Arizona University is situated in beautiful, mountainous Flagstaff, Arizona, a summer/winter recreation area with skiing, hiking, camping, fishing, and boating. Medical facilities for 14,000 students are located in the modern, spacious health center. This academic staff position is 10 months per year. Please address inquiries to Leonard A. Wright, MD, Director, PO Box 6033, Flagstaff, AZ 86011. NAU is an AA/EOE. Women and minority applicants are encouraged to apply.

PHYSICIANS WANTED

NEUROLOGIST

BC/BE, full- or part-time, for expanding San Francisco bay area private practice with emphasis on clinical Occupational Neurology and med-legal evaluations. Expertise in EMG, EEG, and EP desired. Excellent reputation, referral base, facilities, and support staff. Unique income opportunity. Submit CV and letter stating professional goals and availability to:

Personnel
240 Polk St
Box 337
San Francisco, CA 94109

RADIOLOGIST. Immediate opening for BC General and Diagnostic Radiologist at military hospital near Seattle. Washington license not required. Ultrasound, CT, and mammography, plus limited basic angiography and interventional skills. Regular hours. Full-time or six to nine months per year. Five-year contract. Call Dr Bernstein, (213) 521-6630.

ACADEMIC INTERNIST wanted to teach house staff on clinic and inpatient services at LDS Hospital as a member of its Division of General Internal Medicine. ABIM certification and qualifications for University of Utah faculty appointment required. Must have skills and strong interest in teaching, patient care, and research. Start July 1990. Send CV and three letters of recommendation to Corwin Q. Edwards, MD, Clinic Director, LDS Hospital, 8th Ave and Eighth St, Salt Lake City, UT 84143. An Equal Opportunity Employer M/F/H/V. A Facility of Intermountain Health Care, Inc.

DIAGNOSTIC RADIOLOGIST to join five member group covering two small hospitals in northern California. Call (916) 877-8092.

PSYCHIATRIST. Innovative team working with older adults. Med evaluations, consultations. Some supervision. $78K to $104K plus benefits for full-time. Part-time also available. National Institute for Behavior Change, (303) 296-2244. Ask for Lois Munson.

PEDIATRICIANS. At FHP, the nation's largest physician-managed HMO, quality care begins with caring, competent physicians. As a staff physician, you can practice medicine at our Albuquerque medical centers and enjoy competitive salaries with generous benefits. We are currently seeking BC/BE Pediatricians who are quality-minded. Opportunities also are available in Arizona, California, Guam, and Utah. Contact Professional Staffing Dept, 4300 San Mateo NE, Albuquerque, NM 87110; (505) 881-7900 or (800) 444-4347. Equal Opportunity Employer.

ALBUQUERQUE, NEW MEXICO. Physician needed immediately for full-time position in busy Occupational Medicine clinic. Duties include treatment of injured workers, supervision of nurse practitioners, assessment of occupational hazards, etc. BC/BE in Emergency Medicine, Family Practice, Internal Medicine, Occupational Medicine, or Preventive Medicine. Competitive salary and benefits. Send CV to Barry M. Diskant, MD, Albuquerque Industrial Medicine Specialists, PC, 717 Encino Pl, NE, #25, Albuquerque, NM 87102; (505) 842-5151.

BC/BE ORTHOPEDIC SURGEON for beautiful New Mexico mountain community. Camping, fishing, snow skiing, windsurfing, trail-riding, and golf. Low cost of living and high quality of life. Dedicated and compatible hospital staff at progressive JCAH hospital. For further information call Dr Janice Dorn collect, (602) 224-9277, or send inquiry and CV to Janice Dorn, MD, PhD, 4227 N. 32nd St, Ste 108, Phoenix, AZ 85018.

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PHYSICIANS WANTED

OREGON

Excellent opportunity for BC/BE General Internist with large multispecialty group in Portland metropolitan area. Group provides comprehensive medical care to 350,000 members of established northwest HMO. Position offers wide range of Internal Medicine and ample opportunity for subspecialty consultation within collegial professional environment. Competitive salary and benefit package, including generous pension program, sabbatical leave, and professional liability coverage. Forward inquiry and CV to:

Fred M. Nomura, MD
Regional Medical Director
Northwest Permanente, PC
3600 N. Interstate Ave
Portland, OR 97227

SAN FRANCISCO—INTERNAL MEDICINE. Two person Internal Medicine practice seeking BC/BE Internist for immediate association with full partnership in three months. Send résumé to Anhalt Associates Inc, 601 Montgomery St, Ste 1900, San Francisco, CA 94111.

SEEKING A PHYSICIAN to associate with a Family Practice group. Ultramodern facility with outpatient surgical suite. Located in Corona, California, between Orange County and San Diego. Growing area. Good climate. We are offering an association with excellent economic advantage. Contact Ann Holmes, (714) 734-3042.

PULMONOLOGIST, BC/BE to join multispecialty Internal Medicine group in northern California Sierra foothills (one-half hour from Sacramento, one hour from Lake Tahoe). Guaranteed salary/benefits/malpractice with early partnership. Send CV to Number 177, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

SILAS B. HAYES ARMY COMMUNITY HOSPITAL, a 160-bed multispecialty teaching hospital overlooking magnificent Monterey Bay, has rewarding positions: Medical Officer (General Practice), Diagnostic Medical Sonographer, and Diagnostic Radiologic Technician. If interested, call (408) 242-6364/4139 for more information, or visit/write the One-stop Employment Information Center, Bldg 3005, between 10th and 12th St, Fort Ord, CA 93941-5700.

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Redding, the county seat, is a city of 60,000 people located adjacent to the Cascade Mountains in northern California in a semi-rural area. It has outstanding living conditions and a relatively low cost of living.

Contact:

Shasta County Personnel Dept
1500 Court St
Courthouse, Room 105
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Telephone (916) 225-5515

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THE SAN FRANCISCO GENERAL HOSPITAL AIDS PROGRAM of the Department of Medicine of the University of California, San Francisco, seeks an applicant at the Assistant Clinical Professor level. Applicants should have completed a residency in Internal Medicine and be certified by the American Board of Internal Medicine. Additionally, applicants should have received post-residency training in General Internal Medicine or in a subspecialty relevant to AIDS such as Medical Oncology, Infectious Disease, or Clinical Epidemiology. The individual hired will be responsible for the care of AIDS patients, teaching on all levels, and is expected to participate actively in program research activities. Outpatient care is expected to be based in the SFGH AIDS Clinic. Inpatient care will be conducted at SFGH. Applicants should have demonstrated excellence in providing AIDS patient care and in medical teaching. Please submit current CV and three letters of reference to Paul Volberding, MD, Search Committee Chair, AIDS Program, Building 80, Ward 84, San Francisco General Hospital, 995 Potrero Ave, San Francisco, CA 94110. UCSF is an Equal Opportunity/Affirmative Action Employer.

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SAN FRANCISCO BAY AREA. Contemporary General Internist with academic interest sought to join thriving, prestigious private practice on Oakland Pill Hill. Reply to Number 179, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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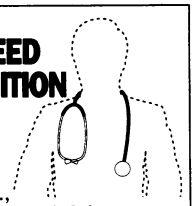

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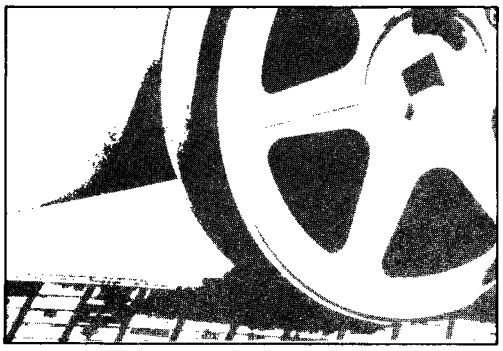

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ranitidine HCl/Glaxo 300 mg tablets

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(ranitidine hydrochloride)
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BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:
1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.
2. Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although ZANTAC has been reported to bind weakly to cytochrome P-450 in vitro, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2,000 mg/kg/day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella, E coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next nine weeks.

Pregnancy: ***Teratogenic Effects: Pregnancy Category B:*** Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ZANTAC. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: ZANTAC is secreted in human milk. Caution should be exercised when ZANTAC is administered to a nursing mother.

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

Use in Elderly Patients: Ulcer healing rates in elderly patients (65 to 82 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with oral ZANTAC®. The relationship to ZANTAC therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to ZANTAC administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

Cardiovascular: Rare reports of tachycardia, bradycardia, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid IV for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Reversible blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. Rare cases of agranulocytosis or of pancytopenia, sometimes with marrow hypoplasia, have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ZANTAC® (ranitidine hydrochloride) and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when ZANTAC has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and rarely, alopecia.

Other: Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

August 1987

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