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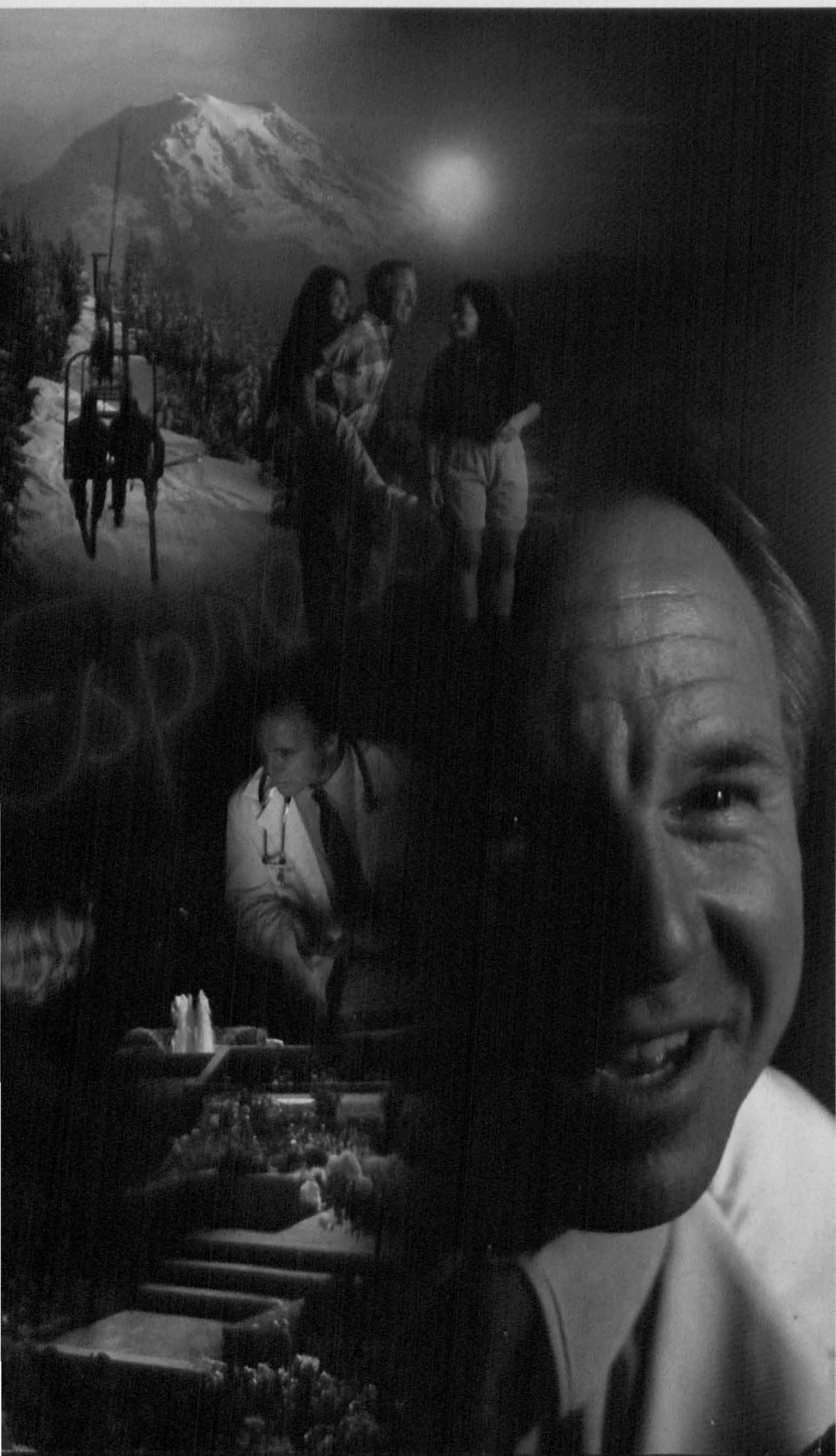
MultiCare's comprehensive system includes two adult hospitals, a nationally recognized pediatric hospital, five day surgery sites, four urgent care centers, a large home health service, and industrial medicine and family practice residency programs. More than 100 primary care and subspecialty physicians have chosen to partner with MultiCare.

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GRAM-NEGATIVE SKIN INFECTIONS  
IN MINOR WOUNDS

- Triple-antibiotic ointment for protection  
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  - Neomycin Sulfate
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skin pathogens

PSEUDOMONAS  
AERUGINOSA

STREPTOCOCCUS  
PYOGENES

ANAEROBIC  
STREPTOCOCCUS

References:

<sup>1</sup> Compared with bacitracin

<sup>2</sup> Change in vehicle only

<sup>3</sup> Data on file (Note: All wounds  
were bandaged.)

<sup>†</sup> Patch sites withdrawn:

2 new Neosporin, 37 previous Neosporin

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AUREUS

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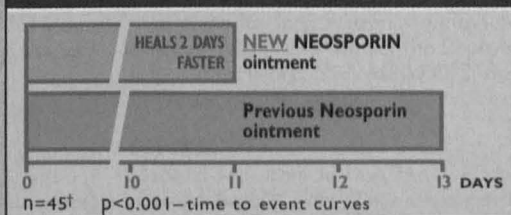
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The American Board of Family Practice invites you to visit its Web site at

*<http://www.abfp.org>*

The site includes the following topics:

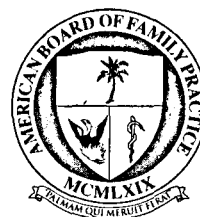
- Requirements for residency training
- Requirements for certification
- Requirements for recertification
- Requirements for Certificates of Added Qualifications in Geriatric Medicine and Sports Medicine
- Future examination dates
- Information on ABFP publications including the *Journal of the American Board of Family Practice*, the *Directory of Diplomates*, and ABFP Reference Guides
- A listing of current and past members of the ABFP Board of Directors
- A staff listing and telephone directory
- The meaning of the ABFP emblem
- Official definitions and policies
- A brief history of the specialty
- Access by city and state to names of ABFP-Certified Family Physicians
- Access by city and state to names of ABFP-Certified Family Physicians with a Certificate of Added Qualifications in Geriatric Medicine
- Access by city and state to names of ABFP-Certified Family Physicians with a Certificate of Added Qualifications in Sports Medicine

We welcome your comments and suggestions.

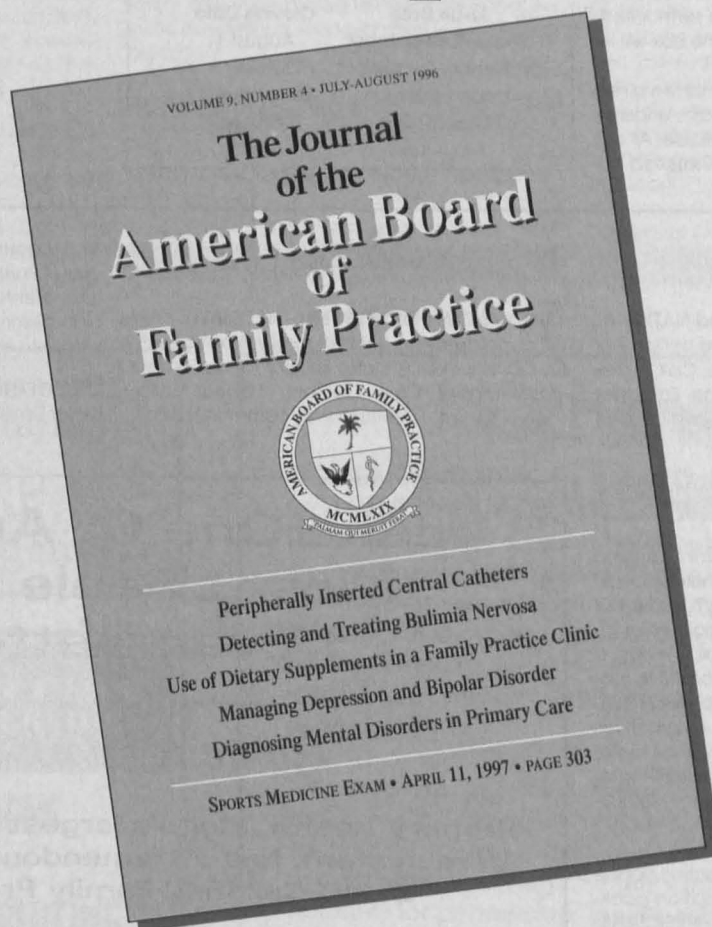
## American Board of Family Practice Inc.

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# The Journal of the American Board of Family Practice

## CLASSIFIED ADVERTISING SECTION

The classified rate is \$1.90 per word (minimum charge of \$80.00 per ad insertion) and \$110.00 per column inch for classified display ads.

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vertisements placed with JABFP are restricted to physician recruitment, faculty positions, CME courses, seminars, and practices for sale. All ads must relate to the medical field and are subject to approval.

Please refer to the schedule below for closing

### Classified Advertising Deadlines

Issue Date	Closing Date
September-October	August 1
November-December	October 1
January-February	December 1
March-April	February 2
May-June	April 1

dates. All advertisements for employment must be nondiscriminatory and comply with all applicable laws and regulations. Ads that discriminate against applicants based on sex, age, race, religion, marital status or physical handicap will not be accepted.

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**FREE TEXAS, SUNBELT, MIDWEST and NATIONAL** career opportunity listings for board certified or eligible Family Practice physicians. Call Bill Pedrey now, 800-736-9490, Search One. Employer inquiries welcome—opportunities available in any state!

### Midwest

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**EAST CENTRAL ILLINOIS** Best of both worlds! Superior Family Practice opportunity in a flourishing

### Northeast

**NORTH CENTRAL PENNSYLVANIA** Want to join a one-, two- or four-person practice where you can concentrate on patient care only? LOOK NO FURTHER! Explore three exciting opportunities affiliated with a progressive hospital, serving a small university community. Easy access to major urban centers, yet located in picturesque, family-oriented recreational areas. All practices provide guaranteed first-year incomes, full benefits and terrific call coverages. Call Foley Proctor Yoskowitz, 800-238-1123 or FAX CV to 973-605-1020.

**NORTHWESTERN NEW JERSEY**—Practice opportunities with competitive compensation package available for BE/BC FAMILY PHYSICIANS. Send CV to: Elizabeth Lejeune, Northwest Covenant Medical Center, SSM Ambulatory Care Corporate Offices, 715 Route 10 East, Randolph, NJ 07869. Fax: 201-442-2330. Phone: 201-442-2307.

### Southeast

**VIRGINIA:** Full-time and part-time board-certified family practice physicians are needed to support the urgent care service associated with the emergency department. Experience preferred. Hours of operation are Monday through Sunday 5 p.m. to 1 a.m. Attractive compensation and benefits. Please send CV to: Emergency Medicine Associates, 9210 Corporate Boulevard, Suite 210, Rockville, Maryland 20850-4697, Attention: Andrea Wergin or facsimile 301-921-7915.

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### Submit CV and questions to:

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community that provides an excellent environment to raise a family. New clinic with the support of an exceptional hospital five minutes away. No OB. Family friendly call schedule. This university community offers many cultural amenities, superb schools, and a healthy economy. Call Adam Jones, 800-243-4353.

**EASTERN WISCONSIN**—Outstanding opportunity for BE/BC FP to reach their full potential. Premiere group has practice in new clinic due to growth. This scenic area has been rated one of the best in the country by both Reader's Digest and Money Magazine. Both Lake Michigan and some of the best golf in the country are very close. Easy access to amenities of large metro area. Desirable call schedule and the support of an excellent hospital. Call Adam Jones 800-243-4353 or 414-241-9500.

**AHEC - FORT SMITH, ARKANSAS** is recruiting a family physician for a full-time faculty position. Community-based, university-administered 6-6-6 Program in community of 75,000 in scenic Arkansas river valley near Ozark and Ouachita Mountains. Temperate climate with four seasons. Duties include teaching residents and

medical students and direct patient care including operative OB. Competitive salary with excellent benefit package. Must be ABFP certified and able to obtain an Arkansas license. Call 501-785-2431 for Jimmy Acklin, M.D., Program Director or L.C. Price, M.D., AHEC Director, or send CV to 612 So.12th St., Fort Smith, AR 72901-4702. EOE.

**WISCONSIN** Join 4 Family Physicians in Oconto Falls, Wisconsin. OB required. Superb quality of life and exceptional outdoor recreational activities abound in this friendly community, just 30 minutes north of Green Bay. Extremely attractive salary and outstanding benefits package. For more information, contact Jackie Laske, 800-243-4353.

#### West

**NORTH IDAHO** Coeur d'Alene area medical clinic for lease or sale, located in one of Idaho's most beautiful and fastest growing areas. Excellent practice opportunity. 208-667-0557 or 208-772-4652.

#### Pacific

#### FACULTY

**OREGON**—Full-time, board-certified faculty needed for Oregon Health Sciences University, Department of Family Medicine. Come and work in a full-time University position, with the Cascades East FMR Program. This unique residency is located in Southern Oregon in a beautiful small city that rests in the Cascade Mountain Range. The program is tailored to provide training for physicians who wish to practice in rural areas of America, and attracts superb residents from throughout the U.S. Come and join a dynamic young faculty who need help in realizing the full potential of a developing program, including resident and medical student teaching, patient care (with obstetrics), with ample opportunity and time to pursue research and administrative duties. A safe environment, good schools and incredible outdoor recreation await the qualified applicant. Please send CV and three references to: James Calvert, MD, or Rob Ross, MD, Cascades East FP Residency Program, 2800 Daggett Avenue, Klamath Falls, OR 97601, or call 541-885-0325 for more information. AA/EEO employer.

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**OCHSNER CLINIC in New Orleans** is searching for a **CHAIRMAN OF THE DEPARTMENT OF FAMILY MEDICINE**. Candidate should be a skilled clinician with excellent organizational and management abilities and experience in residency training. Research in health care delivery preferred but not necessary. The Family Medicine Department has 34 physicians in 12 locations, as well as 17 residents in a free-standing residency program.

Ochsner is a physician owned multi-specialty group practice with over 400 physicians in 23 locations across southeast Louisiana. Ochsner offers a competitive salary, an attractive fringe benefits program, and an opportunity for partnership. Southeast Louisiana offers numerous cultural, historical, and recreational opportunities.

Please send CV to:

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P. O. Box 82109  
Baton Rouge, LA 70884-2109  
Fax (504) 761-5441,  
Information (800) 448-2240,  
E-mail: [dreed@ochsner.org](mailto:dreed@ochsner.org)

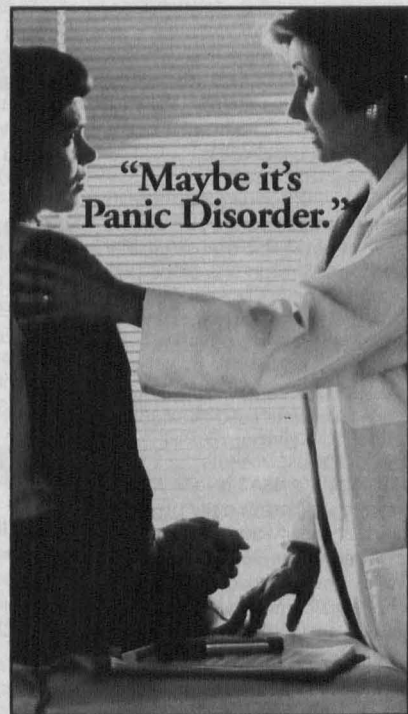
**Gerald Leon Wallace, M.D.**  
**Endowed Chair in Family Medicine**  
**The University of Alabama**  
**School of Medicine**  
**College of Community Health Sciences**  
**Department of Family Medicine**  
**Tuscaloosa, Alabama**

The College of Community Health Sciences and the University of Alabama School of Medicine are proud to announce the creation of the Gerald Leon Wallace, M.D., Endowed Chair in Family Medicine, named in honor and memory of one of Alabama's most distinguished and innovative family physicians. In anticipation of filling this position, we are seeking nominations and applications of individuals who are recognized as outstanding Family Medicine scholars and clinicians and who will qualify at the rank of associate professor or full professor. Qualified applicants will be board certified in family medicine, possess outstanding clinical skills, and have a demonstrated record in research. In addition, we are seeking a person with leadership skills, grantsmanship, and a solid interest in collegial research development consistent with the College's mission. Further qualifications include a commitment to primary care, particularly addressing the needs of rural and underserved areas, and a dedication to the training of family physicians.

The College of Community Health Sciences is a branch campus of the University of Alabama School of Medicine with the mission of providing excellence in the education of 25 third- and 25 fourth-year medical students and in the training of 36 Family Practice residents in family medicine. A major goal of the program is to enhance the accessibility of medical care of rural and underserved populations through the training of competent practitioners. The Department of Family Medicine includes 7 family physicians and 2 non-M.D. faculty. The Tuscaloosa Family Practice Residency has been recognized for more than 20 years as one of the most productive Family Practice Residency programs in the Southeast. The program is affiliated with DCH Regional Medical Center, the third largest hospital in the state, and the Tuscaloosa Veterans Administration Hospital. Capstone Medical Center is the ambulatory care facility for the residency program and manages over 46,000 patient visits annually. The College also offers a competitive Obstetrics Fellowship for family physicians interested in obstetrics as part of their practice.

Tuscaloosa is a community of approximately 100,000 people with many exceptional educational, cultural, and recreational opportunities. The main campus of The University of Alabama, a comprehensive research institution, offers a wide variety of opportunities for faculty and their families.

Send letter of interest and a current curriculum vitae to Jerry McKnight, M.D.; Chairman, Department of Family Medicine; Box 870374; Tuscaloosa, Alabama 35487-0374 or Fax: (205) 348-2889. Applications will be accepted until the position is filled. The University of Alabama is committed to EEO/AA.



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# Practice Life.

For physicians who seek quality in practice and life, Columbia offers America's best opportunities, and options that are virtually limitless. Columbia's sound business management, efficiencies of scale and advanced telecommunications can mean the difference between merely practicing and practicing life.

## BE/BC Family Practitioners

### Alabama

- Southwestern location with mild four-season climate, situated on the areas most sought after recreational waterway. Predictable hours and generous income package—the state provides loan forgiveness. Ref. #T10797BFP.
- Easy access to the sunny gulf coast. Two unique opportunities—join a group of three or be the first in a new three-person office. \$120,000 salary, plus full benefits. New hospital opens in 1998. Ref. #T90797BFP.

### Arkansas

- Join another physician in a safe, secure community of 12,000 in southwest Arkansas, 35 miles from Texarkana. Excellent salary and benefits with six-way call. Outstanding fresh water sports, great hunting. Ref. #D20797BFP.
- Ideal opportunity for family-oriented physician to practice a full range of medicine. Solo practice (including obstetrics) with excellent call arrangements, in a community of 5,000 (service area of 33,000) in southwest Arkansas, 55 miles from Texarkana. Total hospital support. Good schools, low crime rate, fantastic outdoor activities. Ref. #D40797BFP.

### Florida

- Practice life in sunny Florida. If you seek quality in practice and life, Columbia offers an excellent array of private practice and salaried opportunities in many locations throughout the state. You'll enjoy a rewarding business in a warm, semi-tropical paradise, with year-round sun, sailing, golf, fishing and more. Ref. #R40797BFP.

### Kentucky

- Established, expanding group of three seeks a fourth. Southeast city of one million with moderate climate, rolling hills and shopping. Top-notch universities and abundant waterfront recreation. No obstetrics. Ref. #T20797BFP.

### Louisiana

- Join this growing (67,000 patient charts), multi-specialty group between New Orleans and Baton Rouge. Excellent salary, benefits and call. Ref. #D17797BFP.
- Two opportunities exist in this wonderful small city of 128,000 in southern Louisiana (market area of 368,000). Excellent salary, benefits and working conditions. Quality shopping and restaurants, friendly and outgoing people, a low cost-of-living, and an annual growth rate over 6% make this a prime opportunity. Ref. #D22797BFP.
- Dynamic southern city of 200,000 in northwest Louisiana (service area 379,000+). Choice of practice settings, including group, partnership, solo or ER. Extremely fair financial package. Outstanding community offering opera, symphony, theater, a low cost-of-living, low taxes, mild climate, and an excellent quality of life. Ref. #D18797BFP.

### Mississippi

- Sunny gulf coast practice offering a relaxing lifestyle, only 1 1/2 hours to New Orleans. Family Physicians (no obstetrics) and an Occupational Medicine Physician needed. Competitive financial package includes generous salary, relocation and interview expenses. Ref. #T50797BFP.

### Missouri

- Several clinic and private practice opportunities exist in this midwest, family-oriented community serving a southwestern Missouri population of 180,000. Ref. #L40797BFP.

### Nevada

- Practice in Las Vegas, the desert paradise, and become a part of one of the fastest-growing communities in the nation. Salaried and private practice opportunities available. Ref. #L50797BFP.

### Oklahoma

- FP/GP desired to join another in a family-oriented community with a service area of 9,000 in northeast Oklahoma. Excellent salary and benefits combined with great outdoor recreational opportunities (water sports, hiking, hunting, etc.) creates an environment conducive to a healthy lifestyle. Ref. #D00797BFP.
- Practice life in northeast Oklahoma. A salaried position with all benefits and excellent call exists in this all-American town of 20,000, within half an hour of Tulsa. Good family values, friendly community, an annual growth rate of 5%, year round outdoor activities and access to a large city equal a great lifestyle. Ref. #D21797BFP.

### Tennessee

- Minutes away from lakes and waterfalls and within an easy drive from Nashville and Chattanooga. This is an excellent opportunity to serve a population of 35,000 in a new state-of-the-art hospital that rivals any U.S. facility. We have a strong base of business and industry which leads to an excellent payor base. Schools and shopping are outstanding. No state income tax. Ref. #T30797BFP.
- Our location, just over an hour from Nashville in southern Tennessee, is our best kept secret. We serve a population of 40,000 and our hospital is a stand out among its competition by receiving Joint Commission Accreditation with Commendation. Many physicians and executives have homes on the nearby Tennessee river—a favorite place for recreation. Ref. #T40797BFP.
- Sunny Southeast. Our physicians earn in the top 5% of all family physicians in the U.S. Coverage is established and is on a 1 in 5 basis. Practice and live in the dramatic rolling hills located only one hour from Nashville's best shopping mall. Ref. #T70797BFP.

- Our recreational waterways are known all over the Southeast and Midwest. Either join an established practice or be employed by the hospital. Both practices feature 1 in 4 coverage and do not include obstetrics. Ref. #T80797BFP.

- Practice where many people vacation, in this smoky mountain setting located near Knoxville, Tennessee. Population base of 350,000+. Live two minutes from the office in a neighborhood of executive homes or in a mountainside hideaway with a valley view. Abundant recreational opportunities. Salaried positions and income guarantees. Ref. #T10797BFP.

### Texas/Arkansas

- Join our six person FP/IM group serving a community of 65,000 on the beautiful, wooded Texas/Arkansas border. Our rapidly-growing group is three years old. Great area with all amenities and excellent hospital support. Ref. #D50797BFP.

### Texas

- Ground floor opportunity. Join this newly-forming group in an affluent Houston bedroom community. Superb salary, benefits and lifestyle. Ref. #D13797BFP.
- Family Practitioner and Urgent Care Physician needed in this beautiful west Texas city of 92,000, located 90 miles south of Abilene. Big city qualities (symphony, ballet, university and more) without big city problems. You'll enjoy a safe environment with good schools and friendly people. Excellent medical staff and hospital support. Ref. #D8797BFP.

### Utah

- Join established practices or develop new ones in communities along the Wasatch front. Opportunities are available in scenic communities varying in population from 15,000 to 800,000. Practice life in this four-season, family-oriented, outdoor environment. Ref. #L10797BFP.

### West Virginia

- This Mid-Atlantic location features excellent access to beaches, snow skiing, beautiful fall foliage and white water rafting in an area of 250,000. Call 1 in 4. Salary of \$125,000 plus incentive and all overhead costs covered. Ref. #T60797BFP.

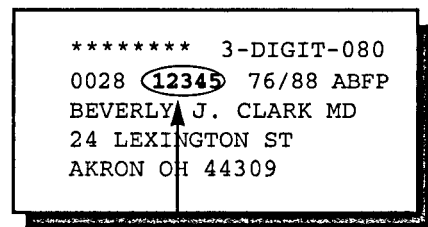
For more information about how you can start practicing life, call on Columbia at 1-888-COLDOCS (1-888-265-3627). Or indicate reference number and send your CV to Columbia Physician Recruitment, One Park Plaza, Nashville, TN, 37203, fax to 1-615-344-2754 or visit our website at <http://www.columbia.net>



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# ATTENTION

## DIPLOMATES OF THE ABFP ADDRESS CHANGE FORM



5-digit ABFP Identification Number

The Board prefers the use of *professional addresses*, because the address given will become your "address of record" with the Board and will be published in our Directory of Diplomates.

Current addresses for all Diplomates are necessary for communication from the Board relating to the Examinations, updated Recertification information, etc., as well as to ensure the receipt of the *Journal of the American Board of Family Practice*.

Name \_\_\_\_\_

**Current Address**

**New Address**

Street \_\_\_\_\_

Street \_\_\_\_\_

City/State \_\_\_\_\_

City/State \_\_\_\_\_

Zip Code \_\_\_\_\_

Zip Code \_\_\_\_\_

Effective Date of Change \_\_\_\_\_

Signature of Diplomate \_\_\_\_\_

ABFP Identification Number \_\_\_\_\_  
(5-digit number above name on mailing label)

Year of Certification or Recertification \_\_\_\_\_

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                              **2228 Young Drive**  
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**Hardworking therapy patients hardly notice**

**References:** 1. Neutel JM, Rolf CN, Valentine SN, et al. Low-dose combination therapy as first-line treatment of mild-to-moderate hypertension. *Cardiovasc Rev Rep.* 1996;17:33-45.  
 2. Zachariah PK, Messerli FH, Mroczek W. Low-dose bisoprolol/hydrochlorothiazide: an option in first-line, antihypertensive treatment. *Clin Ther.* 1993;15:779-787.  
 3. Prisant LM, Weir MR, Papademetriou V, et al. Low-dose drug combination therapy: an alternative first-line approach to hypertension treatment. *Am Heart J.* 1995;130:359-366.  
 4. DeQuattro V, Weir MR. Bisoprolol fumarate/hydrochlorothiazide 6.25 mg: a new low-dose option for first-line antihypertensive therapy. *Adv Ther.* 1993;10:197-206.

**Brief Summary**

**ZIAC<sup>®</sup> (Bisoprolol Fumarate and Hydrochlorothiazide) Tablets**

FOR FULL PRESCRIBING INFORMATION, PLEASE CONSULT PACKAGE INSERT.

**DESCRIPTION**

ZIAC (bisoprolol fumarate and hydrochlorothiazide) is indicated for the treatment of hypertension. It combines two antihypertensive agents in a once-daily dosage: a synthetic beta<sub>1</sub>-selective (cardioselective) adrenoceptor blocking agent (bisoprolol fumarate) and a benzothiadiazine diuretic (hydrochlorothiazide).

**CLINICAL PHARMACOLOGY**

At doses ≥ 20 mg bisoprolol fumarate inhibits beta<sub>1</sub>-adrenoreceptors located in bronchial and vascular musculature. To retain relative selectivity, it is important to use the lowest effective dose.

**CONTRAINDICATIONS**

Cardiogenic shock, overt cardiac failure (see WARNINGS), second- or third-degree AV block, marked sinus bradycardia, anuria, and hypersensitivity to either component of this product or to other sulfonamide-derived drugs.

**WARNINGS**

**Cardiac Failure:** Beta-blocking agents should be avoided in patients with overt congestive failure. **Patients Without a History of Cardiac Failure:** Continued depression of the myocardium with beta-blockers can precipitate cardiac failure. At the first signs or symptoms of heart failure, discontinuation of ZIAC should be considered.

**Abrupt Cessation of Therapy:** Abrupt cessation of beta-blockers should be avoided. Even in patients without overt coronary artery disease, it may be advisable to taper therapy with ZIAC over approximately 1 week with the patient under careful observation. If withdrawal symptoms occur, beta-blocking agent therapy should be reinstated, at least temporarily.

**Peripheral Vascular Disease:** Beta-blockers should be used with caution in patients with peripheral vascular disease.

**Bronchospastic Disease:** PATIENTS WITH BRONCHOSPASTIC PULMONARY DISEASE SHOULD, IN GENERAL, NOT RECEIVE BETA-BLOCKERS.

**Anesthesia and Major Surgery:** If used perioperatively, particular care should be taken when anesthetic agents that depress myocardial function, such as ether, cyclopropane, and trichloroethylene, are used.

**Diabetes and Hypoglycemia:** Beta-blockers may mask some of the manifestations of hypoglycemia, particularly tachycardia. Patients subject to spontaneous hypoglycemia, or diabetic patients receiving insulin or oral hypoglycemic agents, should be cautioned. Also, latent diabetes mellitus may become manifest and diabetic patients given thiazides may require adjustment of their insulin dose.

**Thyrotoxicosis:** Beta-adrenergic blockade may mask clinical signs of hyperthyroidism. Abrupt withdrawal of beta-blocker may be followed by an exacerbation of the symptoms of hyperthyroidism or may precipitate thyroid storm.

**Renal Disease:** Cumulative effects of the thiazides may develop in patients with impaired renal function. In such patients, thiazides may precipitate azotemia. In subjects with creatinine clearance less than 40 mL/min, the plasma half-life of bisoprolol fumarate is increased up to threefold, as compared to healthy subjects.

**Hepatic Disease:** ZIAC should be used with caution in patients with impaired hepatic function or progressive liver disease.

**PRECAUTIONS**

**General: Electrolyte and Fluid Balance Status:** Periodic determination of serum electrolytes should be performed, and patients should be observed for signs of fluid or electrolyte disturbances. Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

Hypokalemia may develop. Hypokalemia and hypomagnesemia can provoke ventricular arrhythmias or sensitize or exaggerate the response of the heart to the toxic effects of digitalis.

Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than salt administration, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

**Parathyroid Disease:** Calcium excretion is decreased by thiazides, and pathologic changes in the parathyroid glands, with hypercalcemia and hypophosphatemia, have been observed in a few patients on prolonged thiazide therapy.

**Hyperurcemia:** Hyperuricemia or acute gout may be precipitated in certain patients receiving thiazide diuretics. Bisoprolol fumarate, alone or in combination with HCTZ, has been associated with increases in uric acid.

**Drug Interactions:** ZIAC may potentiate the action of other antihypertensive agents used concomitantly. ZIAC should not be combined with other beta-blocking agents. In patients receiving concurrent therapy with clonidine, if therapy is to be discontinued, it is suggested that ZIAC be discontinued for several days before the withdrawal of clonidine.

ZIAC should be used with caution when myocardial depressants or inhibitors of AV conduction or antiarrhythmic agents are used concurrently.

**Bisoprolol Fumarate:** Concurrent use of rifampin increases the metabolic clearance of bisoprolol fumarate, shortening its elimination half-life. Pharmacokinetic studies do not clinically relevant interactions with other agents given concomitantly, including thiazide diuretics, digoxin and cimetidine. There was no effect of bisoprolol fumarate on prothrombin times in patients on stable doses of warfarin.

**Risk of Anaphylactic Reaction:** While taking beta-blockers, patients with a history of severe anaphylactic reaction may be more reactive to repeated challenge, either accidental, diagnostic, or therapeutic and may be unresponsive to the usual doses of epinephrine used to treat allergic reactions.

**Hydrochlorothiazide:** The following drugs may interact with thiazide diuretics. Alcohol, barbiturates, or narcotics—potentiation of orthostatic hypotension may occur. Dosage adjustment of the antidiabetic drugs (oral agents and insulin) may be required. Other antihypertensive drugs—additive effect or potentiation. Cholestyramine and colestipol resins—single doses of cholestyramine and colestipol resins bind the hydrochlorothiazide and reduce its absorption in the gastrointestinal tract by up to 85 percent and 43 percent, respectively. Corticosteroids, ACTH—intensified electrolyte depletion, particularly hypokalemia. Possible decreased response to pressor amines but not sufficient to preclude their use. Possible increased responsiveness to muscle relaxants, nondepolarizing. Generally, lithium should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. The administration of a nonsteroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics.

In patients receiving thiazides, sensitivity reactions may occur with or without a history of allergy or bronchial asthma. Photosensitivity reactions and possible exacerbation or activation of systemic lupus erythematosus have been reported in patients receiving thiazides. The antihypertensive effects of thiazides may be enhanced in the post-sympathectomy patient.

**Laboratory Test Interactions:** Based on reports involving thiazides, ZIAC may decrease serum levels of protein-bound iodine without signs of thyroid disturbance. Because it includes a thiazide, ZIAC should be discontinued before carrying out tests for parathyroid function (see PRECAUTIONS—Parathyroid Disease).

**ADVERSE REACTIONS**

ZIAC: Bisoprolol fumarate/H6.25 mg is well tolerated in most patients. Most adverse effects (AEs) have been mild and transient. In more than 65,000 patients treated worldwide with bisoprolol fumarate, occurrences of bronchospasm have been rare. Discontinuation rates for AEs were similar for B/H6.25 mg and placebo-treated patients. In the United States, 252 patients received bisoprolol fumarate (2.5, 5, 10, or 40 mg)/H6.25 mg and 144 patients received placebo in two controlled trials. In Study 1, bisoprolol fumarate 5/H6.25 mg was administered for 4 weeks. In Study 2, bisoprolol fumarate 2.5, 10 or 40/H6.25 mg was administered for 12 weeks. All adverse experiences, whether drug-related or not, and drug-related adverse experiences in patients treated with B2.5-10/H6.25 mg, reported during comparable, 4 week treatment periods by at least 2% of bisoprolol fumarate/H6.25 mg-treated patients (plus additional selected adverse experiences) are presented in the following table:

**ZIAC<sup>®</sup> (Bisoprolol Fumarate and Hydrochlorothiazide) Tablets**

% of Patients with Adverse Experiences\*

Body System/ Adverse Experience	All Adverse Experiences		Drug-Related Adverse Experiences	
	Placebo <sup>1</sup> (n=144) %	B2.5-10/H6.25 <sup>1</sup> (n=252) %	Placebo <sup>1</sup> (n=144) %	B2.5-10/H6.25 <sup>1</sup> (n=251) %
<b>Cardiovascular</b>				
bradycardia	0.7	1.1	0.7	0.9
arrhythmia	1.4	0.4	0.0	0.0
peripheral ischemia	0.9	0.7	0.9	0.4
chest pain	0.7	1.8	0.7	0.9
<b>Respiratory</b>				
bronchospasm	0.0	0.0	0.0	0.0
cough	1.0	2.2	0.7	1.5
rhinitis	2.0	0.7	0.7	0.9
URI	2.3	2.1	0.0	0.0
<b>Body as a Whole</b>				
asthenia	0.0	0.0	0.0	0.0
fatigue	2.7	4.6	1.7	3.0
peripheral edema	0.7	1.1	0.7	0.9
<b>Central Nervous System</b>				
dizziness	1.8	5.1	1.8	3.2
headache	4.7	4.5	2.7	0.4
<b>Musculoskeletal</b>				
muscle cramps	0.7	1.2	0.7	1.1
myalgia	1.4	2.4	0.0	0.0
<b>Psychiatric</b>				
insomnia	2.4	1.1	2.0	1.2
somnolence	0.7	1.1	0.7	0.9
loss of libido	1.2	0.4	1.2	0.4
impotence	0.7	1.1	0.7	1.1
<b>Gastrointestinal</b>				
diarrhea	1.4	4.3	1.2	1.1
nausea	0.9	1.1	0.9	0.9
dyspepsia	0.7	1.2	0.7	0.9

\*Averages adjusted to combine across studies.

<sup>1</sup>Combined across studies.

Other adverse experiences that have been reported with the individual components are listed below.

**Bisoprolol Fumarate:** In clinical trials worldwide, a variety of other AEs, in addition to those listed above, have been reported. While in many cases it is not known whether a causal relationship exists between bisoprolol and these AEs, they are listed to alert the physician to a possible relationship. **Central Nervous System:** Unsteadiness, vertigo, syncope, paresthesia, hyperesthesia, sleep disturbance/vivid dreams, depression, anxiety/restlessness, decreased concentration/memory. **Cardiovascular:** Palpitations and other rhythm disturbances, cold extremities, claudication, hypotension, orthostatic hypotension, chest pain, congestive heart failure. **Gastrointestinal:** Gastric/epigastric/abdominal pain, peptic ulcer, gastritis, vomiting, constipation, dry mouth. **Musculoskeletal:** Arthralgia, muscle/joint pain, back/neck pain, twitching/tremor, skin. **Skin:** Rash, acne, eczema, psoriasis, skin irritation, pruritus, purpura, flushing, sweating, alopecia, dermatitis, exfoliative dermatitis (very rarely), cutaneous vasculitis. **Special Senses:** Visual disturbances, ocular pain/pressure, abnormal lacrimation, tinnitus, decreased hearing, earache, taste abnormalities. **Metabolic:** Gout. **Respiratory:** Asthma, bronchitis, dyspnea, pharyngitis, sinusitis. **Genitourinary:** Peyronie's disease (very rarely), cystitis, renal colic, polyuria. **General:** Malaise, edema, weight gain, angioedema.

In addition, a variety of adverse effects have been reported with other beta-adrenergic blocking agents and should be considered potential adverse effects: **Central Nervous System:** Reversible mental depression progressing to catatonia, hallucinations, an acute reversible syndrome characterized by disorientation to time and place, emotional lability, slightly clouded sensorium. **Allergic:** Fever, combined with aching and sore throat, laryngospasm, and respiratory distress. **Hematology:** Agranulocytosis, thrombocytopenia. **Gastrointestinal:** Mesenteric arterial thrombosis and ischemic colitis. **Miscellaneous:** The oculomucocutaneous syndrome associated with the beta-blocker procarbamol has not been reported with bisoprolol fumarate during investigational use or extensive foreign marketing experience.

**Hydrochlorothiazide:** The following adverse experiences, in addition to those listed in the above table, have been reported with hydrochlorothiazide (generally with doses of 25 mg or greater). **General:** Weakness. **Central Nervous System:** Vertigo, paresthesia, restlessness. **Cardiovascular:** Orthostatic hypotension (may be potentiated by alcohol, barbiturates, or narcotics). **Gastrointestinal:** Anorexia, gastric irritation, cramping, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, cholelithiasis, sialadenitis, dry mouth. **Musculoskeletal:** Muscle spasm. **Hypersensitive Reactions:** Purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions. **Special Senses:** Transient blurred vision, xanthopsia. **Metabolic:** Gout. **Genitourinary:** Sexual dysfunction, renal failure, renal dysfunction, interstitial nephritis.

**LABORATORY ABNORMALITIES**

**ZIAC:** Because of the low dose of hydrochlorothiazide in ZIAC, adverse metabolic effects with B/H6.25 mg are less frequent and of smaller magnitude than with HCTZ 25 mg.

Treatment with both beta-blockers and thiazide diuretics is associated with increases in uric acid. Mean increases in serum triglycerides were observed in patients treated with bisoprolol fumarate and hydrochlorothiazide 6.25 mg. Total cholesterol was generally unaffected, but small decreases in HDL cholesterol were noted.

Other laboratory abnormalities that have been reported with the individual components are listed below. **Bisoprolol Fumarate:** In clinical trials, the most frequently reported laboratory change was an increase in serum triglycerides, but this was not a consistent finding.

Sporadic liver test abnormalities have been reported. In the U.S. controlled trials experience with bisoprolol fumarate treatment for 4 to 12 weeks, the incidence of concomitant elevations in SGOT and SGPT of between 1 to 2 times normal was 3.9%, compared to 2.5% for placebo. No patient had concomitant elevations greater than twice normal.

In the long-term, uncontrolled experience with bisoprolol fumarate treatment for 6 to 18 months, the incidence of one or more concomitant elevations in SGOT and SGPT of between 1-2 times normal was 6.2%. The incidence of multiple occurrence was 1.9%. For concomitant elevations in SGOT and SGPT of greater than twice normal, the incidence was 1.5%. The incidence of multiple occurrences was 0.3%. In many cases these elevations were attributed to underlying disorders, or resolved during continued treatment with bisoprolol fumarate.

Other laboratory changes included small increases in uric acid, creatinine, BUN, serum potassium, glucose, and phosphorus and decreases in WBC and platelets. There have been occasional reports of eosinophilia. These were generally not of clinical importance and rarely resulted in discontinuation of bisoprolol fumarate.

As with other beta-blockers, ANA conversions have also been reported on bisoprolol fumarate. About 15% of patients in long-term studies converted to a positive titer, although about one-third of these patients subsequently reconverted to a negative titer while on continued therapy.

**Hydrochlorothiazide:** Hyperglycemia, glycosuria, hyperuricemia, hypokalemia and other electrolyte imbalances (see PRECAUTIONS), hyperlipidemia, hypercalcemia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, and hemolytic anemia have been associated with HCTZ therapy.

See **DOSAGE AND ADMINISTRATION** section in package insert for complete dosing and precautionary information.



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CI 4567-1  
 Issued October 11, 1995



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