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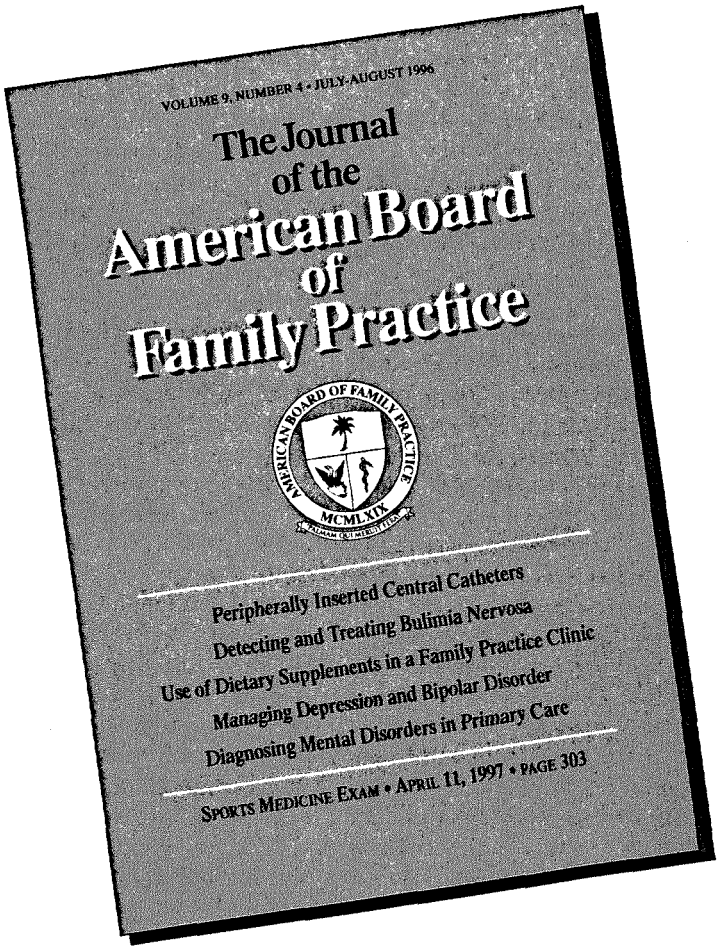

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The Journal of the American Board of Family Practice

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Northeast

FAMILY PRACTICE—SOUTHWESTERN PENNSYLVANIA—Four Board Certified physicians seek BE/BC associate for well-established and expanding practice. Enjoy working in a large, modern office with lab and x-ray capabilities. Live in a community which provides quality, affordable housing, excellent schools and easy access to Pittsburgh's sports and cultural amenities. Excellent compensation/benefit package. For more information, please call Elaine Bolanis at Daniel Stern and Associates at 1-800-438-2476 or FAX 1-800-892-2781.

FINGER LAKES, NEW YORK: BC/BE. Family practice in small rural community. Spectacular surroundings. Well-trained group with one/six call. Opportunity for University of Rochester faculty position in rural family practice residency program. Generous salary or practice guarantee. Fax CV: 315-536-0897 or send CV to Sheila McMichael, 418 North Main Street, Penn Yan, NY 14527.

NEW HAMPSHIRE (SOUTHERN): Join a primary care group of 6 physicians in the beautiful Capital Region one hour from Boston. 1:5 call. 250+ bed regional referral hospital. Base salary with incentive and benefits. Contact Doug Page by phone (800-238-7150), fax (610-975-0574) or e-mail (103725.3572@compuserve.com).

NEW JERSEY (CENTRAL): Join an expanding primary care group of 7 FP's and IM's in Monmouth County—close to New York City and the Jersey Shore. Group is replacing a retiring physician and opening a new office. Employed position with salary plus incentives and benefits. Contact Doug Page by phone (800-238-7150), fax (610-975-0574) or e-mail (103725.3572@compuserve.com).

PENNSYLVANIA (CENTRAL): Take over existing practice of retiring physician with no business hassles. $120,000 annually plus incentives and full benefits. School loan repayment program available. College town (and only 30 minutes from Penn State/State College) with 100+ bed acute care hospital with National Affiliation. 1:6 Call. Contact Doug Page by phone (800-238-7150), fax (610-975-0574) or e-mail (103725.3572 @compuserve.com).

PENNSYLVANIA (SOUTH CENTRAL)—OUTPATIENT ONLY: Family Practice group in York County with 5 physicians seeking a 6th. Quality medicine in efficient working environment in a very attractive community. Salary, incentive, and full benefit package. Contact Doug Page by phone (800-238-7150), fax (610-975-0574) or e-mail (103725. 3572@compuserve.com).

PENNSYLVANIA—STATE COLLEGE AREA: 16 physician multispecialty group looking to add sixth Family Practice physician. New office location across street from hospital. Base salary, incentive bonus, excellent benefits including malpractice and retirement. Contact David Finney, Howe, Lawlor and Associates at 800-238-7150 or fax CV to 610-975-0574, or e-mail (103725.3572@ compuserve.com).

CHAIR
DEPARTMENT OF FAMILY MEDICINE

The SUNY Health Science Center at Syracuse seeks a new Chair for the Department of Family Medicine. The Department has a long history of excellence in medical education and patient care. The Department operates two residency programs (St. Joseph's and Crouse-Irving Memorial-PHP) and coordinates the Introduction to Clinical Medicine course for the Medical School. A Family Medicine clerkship is in the planning phases. The Department also sponsors the Rural Medicine (RMED) program which places medical students in rural practices in central New York for a major portion of their third year.

The Committee seeks an outstanding Family Physician with strong academic qualifications to oversee the broad clinical and educational activities of the Department and to develop additional educational, academic, and clinical service programs within the Health Science Center.

Applicants must be appropriate for appointment at the Associate or Professor level. Syracuse is located in central New York and has excellent cultural, professional, and recreational activities. The area has been ranked amongst the best metropolitan areas to live in by the *Places Rated Almanac* and has excellent schools and a low crime rate.

Please send CV to: Ms. Barbara Ames
Provost Office, WSK
SUNY Health Science Center
750 East Adams Street
Syracuse, New York 13210

Women and minority applicants are especially encouraged to apply.

State University of New York
Health Science Center
Syracuse

PHILADELPHIA: Nationally known 600+ bed Regional Trauma Center, with expanding primary care network, is recruiting for Family Practice Physicians in Philadelphia. Join 21 physician multispecialty group with community based offices. Salary, incentives and benefits. Contact Doug Page by phone (800-238-7150), fax 610-975-0574) or e-mail (103725.3572 @compuserve.com).

RHODE ISLAND: Join primary care physicians serving prosperous 350+ bed medical center less than 1 hour from Boston. 1:6 call. Partnership track and 6 figure salary, 3 year forgivable guarantee with benefits. Contact Doug Page by phone (800-238-7150), fax (610-975-0574) or e-mail (103725.3572@compuserve.com).

SOUTHWESTERN PA. Family Practice. An excellent opportunity exists for a BE/BC FP to practice both clinical and academic medicine. Enjoy a private practice located in a quaint semi-rural community south of Pittsburgh. This opportunity provides an outstanding cross-coverage relationship with other faculty members. This person will also be involved with teaching medical students and family practice residents in an outstanding program sponsored by a mid-sized community hospital. Excellent compensation/benefits. For more information, please contact Elaine Bolanis at: Daniel Stern and Associates, The Medical Center East, 211 N. Whitfield Street, Pittsburgh, PA 15206. Call 1-800-438-2476 or fax 1-800-892-2781.

Southeast

DEPARTMENT OF FAMILY MEDICINE—The Department of Family Medicine at the Medical University of South Carolina is currently seeking a board-certified family physician. The successful applicant will be actively involved in clinical practice (80%), teaching (20%) and will have the opportunity to pursue scholarly and intellectual interests in a stimulating and supportive environment. This university-based department is located in Charleston, SC, a beautiful coastal city with a charming historic downtown area. The Medical University of South Carolina is an EOE/AA employer. Interested individuals may direct inquiries and CVs to A.C. Hutson, MD, Chairman, Department of Family Medicine, Medical University of South Carolina, 171 Ashley Avenue, Charleston, SC 29425.

FACULTY POSITION: The Department of Family Medicine at The University of Alabama School of Medicine, Tuscaloosa Program is seeking an Assistant or Associate Professor for a clinical or tenure track position. Responsibilities in this well-established 36 resident program include resident and medical student teaching, patient care, research, and scholarly activity. Applicants must be ABFP-certified and residency trained and must hold or be eligible for Alabama medical licensure. Tuscaloosa is a growing university town with numerous educational, cultural, and recreational opportunities. Send CV to Jerry McKnight, M.D., Department of Family Medicine, Box 870374, Tuscaloosa, AL 35487-0374. AA/EOE.

WANTED: BC/BE FAMILY PRACTITIONER, preferably with occupational medicine background, to work at a Family Practice Office in Charleston, South Carolina. 3-5 years practice experience preferable but not necessary. Must be willing to work evenings until 9 pm and share in call schedule of a busy 3 FP practice. This practice is managed by Carolina Family Care, a branch of the faculty practice plan of the Medical University of South Carolina. We offer a pleasant work environment, competitive salary, and extensive fringe benefit package, plus the opportunity to grow in a busy practice. Please send all inquiries to: Howard A. Evert, MD, President, Carolina Family Care, 1 Poston Rd., Suite 110, Charleston, SC 29407.

Midwest

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 Larry L. Hanley, 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.

ASSISTANT/ASSOCIATE/PROFESSOR: The University of South Dakota School of Medicine, a family practice oriented school, is seeking both junior and experienced faculty for its expanding Department of Family Medicine. Applicants must be residency trained and board certified, and be eligible for licensure in the State of South Dakota. The Department of Family Medicine has required courses/clerkships in all four years of the curriculum, and will be responsible for directing a developing longitudinal primary care ambulatory program. A number of departmental leadership positions are available depending upon qualifications and experience. Responsibilities will include teaching, patient care and scholarly activity. Rank and compensation will be commensurate with qualifications and experience. Applications will be reviewed starting April 1, 1996, and continue until suitable candidates are hired. Send CV to H. Bruce Vogt, M.D., Chair, Department of Family Medicine, 1400 W. 22nd Street, Sioux Falls, SD 57105-1570, AA/EOE.

BC/FAMILY PRACTICE PHYSICIAN—Liberty Healthcare Corp. seeks a qualified physician for our ambulatory care setting NW of Des

Moines, IA. You will be providing primary care to employees/dependents of a major corporation. Grow into a leadership role in a premier practice setting. Excellent compensation, generous paid time off, stable 40-hour, Mon-Fri schedule. Contact Connie Grazel, Liberty Healthcare Corporation, 401 City Ave., Suite 820, Bala Cynwyd, PA 19004; 800-331-7122; 24-hour line 610-617-3699, ext. 157; fax 610-667-5559. EOE.

DEAN, GRADUATE MEDICAL EDUCATION—Associate Professor/Professor, Family Medicine— The University of South Dakota School of Medicine, a family practice-oriented school, is seeking an experienced family physician to serve as Dean of Graduate Medical Education and as a member of the Department of Family Medicine. Applicants must be residency trained and board certified and be eligible for licensure in the state of South Dakota. The Department of Family Medicine has required courses/clerkships in all 4 years of the curriculum. The School has affiliated family practice residency programs in Sioux Falls, Rapid City, and two Rural Track Programs. The School also has residency programs in internal medicine, pathology, general psychiatry, child and adolescent psychiatry, and transitional year. Responsibilities will include administration, teaching, patient care, and scholarly activity. Rank and compensation will be commensurate with qualifications and experience. Applications will be reviewed starting July 1, 1996 and continue until a suitable candidate is hired. Send CV to Rod Parry, MD, Executive Dean, 1400 W. 22nd Street, Sioux Falls, SD 57105-1570.

STRELCHECK & ASSOCIATES offers a variety of desirable settings complementing your lifestyle! You owe it to yourself to evaluate these exceptional opportunities. Progressive multispecialty groups and a staff model HMO are seeking additional family physicians in Wisconsin, Iowa, and Michigan. Practice state-of-the-art health care with friendly progressive colleagues at well established clinics with liberal call coverage and comprehensive salary/benefits. Now is the time to take initiative! Call Jackie Laske at (800) 243-4353.

UNIVERSITY OF ILLINOIS AT CHICAGO, DEPARTMENT OF FAMILY MEDICINE is seeking ABFP-certified family physician as associate or full professor for teaching, research, management, and clinical responsibilities for newly developing nearby community practice in a Mexican American neighborhood. Must be bilingual Spanish/English, experienced in FP education and working with Latino communities. Faculty will be fully integrated into departmental activities and considered senior and central to the department. Contact Elizabeth Burns, MD, MA, Head, Department of Family Medicine (M/C663), UIC, 1919 W. Taylor Street, Chicago, IL 60612-7248. AA/EOE.

West

FAMILY PHYSICIAN FACULTY—The Family Practice Residency of Idaho is a 27-resident, fully accredited, community hospital-based program affiliated with the University of Washington School of Medicine. Program provides excellent training for physicians wishing to practice in rural areas. Candidate must be ABFP Certified/Board Eligible. Previous teaching and/or practice experience is required. Responsibilities include teaching and supervising residents, patient care, including obstetrics. Boise is located near all types of outdoor recreational activities and offers the cultural advantages of a small university city. Excellent salary and benefits. Contact Karl Watts, MD, Interim Director, Family Practice Residency of Idaho, 777 N. Raymond Street, Boise, ID 83704, 208-322-0050.

GET A LIFE! COME TO MONTANA: Live in beautiful Montana and enjoy the best life has to offer! Excellent opportunity for a talented, dedicated BC/BE family practitioner to be part of a newly established and growing community health center providing care to primarily medicaid/low-to-moderate income patients. We are located in beautiful Great Falls, Montana, with ready access to outdoor recreation activities, good schools, and affordable housing. Excellent salary and full benefits. Shared call, beautiful facility, state-of-the-art equipment, generous support staff including a social worker and your own full-time nurse. We offer all this and more, along with the satisfaction of knowing that you can make a profound impact on the health and well-being of your patients and the community. Interested physicians should contact Cherry Loney, Executive Director, City-County Health Department, 1130 17th Avenue South, Great Falls, Montana 59405. Phone (406) 454-6950; fax (406) 454-6959. E.O.E.

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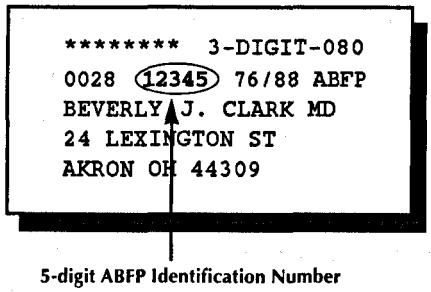

The Board prefers the use of *professional addresses,* because the address given will become your "address of record" with the Board and will be published in our Directory of Diplomates.

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**
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2228 Young Drive
Lexington, KY 40505

First-line therapy option

ZIAC®

(bisoprolol fumarate-hydrochlorothiazide)
2.5, 5, & 10 mg Tablets with 6.25 mg HCTZ

References:

1. 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. **2.** Data on file. Lederle Laboratories, Pearl River, NY. **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.** Zachariah PK, Messerli FH, Mroczek W. Low-dose bisoprolol/hydrochlorothiazide: an option in first-line, antihypertensive treatment. *Clin Ther.* 1993;15:779-787.

Brief Summary

ZIAC® (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$_1$-selective (cardioselective) adrenoceptor blocking agent (bisoprolol fumarate) and a benzothiadiazine diuretic (hydrochlorothiazide).

CLINICAL PHARMACOLOGY

At doses ≥ 20 mg bisoprolol fumarate inhibits beta$_1$-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 reinstituted, 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-blockade 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.

Hyperuricemia: 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 document no 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® (Bisoprolol Fumarate and Hydrochlorothiazide) Tablets

Body System/ Adverse Experience	% of Patients with Adverse Experiences*			
	All Adverse Experiences		Drug-Related Adverse Experiences	
	Placebo† (n = 144) %	B2.5-40/H6.25† (n = 252) %	Placebo† (n = 144) %	B2.5-10/H6.25† (n = 221) %
Cardiovascular				
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
Respiratory				
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
Body as a Whole				
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
Central Nervous System				
dizziness	1.8	5.1	1.8	3.2
headache	4.7	4.5	2.7	0.4
Musculoskeletal				
muscle cramps	0.7	1.2	0.7	1.1
myalgia	1.4	2.4	0.0	0.0
Psychiatric				
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
Gastrointestinal				
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.
† 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:* 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. *Hematologic:* Agranulocytosis, thrombocytopenia. *Gastrointestinal:* Mesenteric arterial thrombosis and ischemic colitis. *Miscellaneous:* The oculomucocutaneous syndrome associated with the beta-blocker practolol 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, cholecystitis, sialadenitis, dry mouth. *Musculoskeletal:* Muscle spasm. *Hypersensitive Reactions:* Purpura, photosensitivity, rash, urticaria, necrotizing angiitis (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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