Low-dose composition minimizes overall incidence of side effects

- ZIAC avoids beta-blocker-associated side effects
  - The two most common side effects—dizziness (3.2%) and fatigue (3.0%)—occurred at rates comparable to placebo
- ZIAC has a low incidence of cough (1.5%), peripheral edema (0.9%), and headache (0.4%)—which occurred at rates comparable to placebo

Up to 80% of patients controlled with equivalent efficacy regardless of age, race, or gender

ZIAC is contraindicated in patients in cardiogenic shock, overt cardiac failure, second- or third-degree AV block, marked sinus bradycardia, anuria, and hypersensitivity to either component of this product or to other sulfonamide-derived drugs.

*Clinical trial response rates were: 2.5 mg—61%; 5 mg—73%; 10 mg—80%.
Please see Brief Summary of Prescribing Information on adjacent page.
Ziac® (Bisoprolol Fumarate and Hydrochlorothiazide) Tablets

**DESCRIPTION**
Ziac® (bisoprolol fumarate and hydrochlorothiazide) is indicated for the treatment of hypertension. It combines two antihypertensive agents in a single oral dose: a beta-adrenergic blocking agent (bisoprolol fumarate) and a thiazide diuretic (hydrochlorothiazide).

**CLINICAL PHARMACOLOGY**
At doses of 20 mg bisoprolol fumarate inhibits beta-adrenergic receptors 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 atrioventricular block unless a pacemaker is in place. Severe uncontrolled asthmatic or bronchospastic episodes. Severe hepatic or renal disease.

**WARNINGS**
Failure: Beta-blockers should be avoided in patients with overt congestive failure. Patients with bronchospastic disease should, in addition, be used with caution.

**BENIGN BRONCHIAL PULMONARY DISEASE**: Patients with bronchospastic disease should, in addition, be used with caution.

**ADVERSE REACTIONS**
Laboratory Test Abnormalities: To retain relative selectivity, it is important to use the lowest effective dose.

Body System/Adverse Experience

<table>
<thead>
<tr>
<th>% of Patients with Adverse Experiences*</th>
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<td>Drug-Related Adverse Experiences</td>
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* Averages obtained to combine across studies.

Combined across studies.

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

Beta-blockers: 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: Dizziness, vertigo, nervousness.

**WARNINGS**
Failure: Beta-blockers should be avoided in patients with overt congestive failure. Patients with bronchospastic disease should, in addition, be used with caution.

**BENIGN BRONCHIAL PULMONARY DISEASE**: Patients with bronchospastic disease should, in addition, be used with caution.

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References:

Drug Interactions:
ESGC-PLUS Tablets: Butalbitol is habit-forming and potentially abuseable. Consequently, the extended use of this product is not recommended.

PRECAUTIONS:
General: Butalbitol Tablets should be prescribed with caution to patients with a history of cerebrovascular disease, those with severe liver disease, or those with active peptic ulcer disease. Butalbitol Tablets may be habit-forming and potentially abuseable. Consequently, the extended use of this product is not recommended.

ADVERSE REACTIONS:
Butalbitol Tablets are well tolerated by the usual adult patient. The most frequently reported adverse reactions are drowsiness, light-headedness, dizziness, sedation, somnolence, dizziness, nausea, vomiting, abdominal pain, and irritability.

WARNINGS:
Butalbitol Tablets may be habit-forming and potentially abuseable. Consequently, the extended use of this product is not recommended.

DRUG ABUSE AND DEPENDENCE: Abuse and Dependence: Butalbitol: Butalbitol Tablets may be habit-forming. Tolerance to the effects of Butalbitol Tablets may occur, especially following prolonged use at high doses of Butalbitol. The average daily dose for the Butalbitol addict is usually more than 1500 mg. The maximum daily dose of Butalbitol tablets is 600 mg. As tolerance to Butalbitol develops, the amount of time it takes to attain any given level of intoxication is decreased and the duration of action is decreased. Therefore, the amount of time it takes to attain an intoxication of any given level is decreased, and the duration of action is decreased.

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MICHIGAN — War Memorial Hospital in Sault Ste. Marie, Michigan is assisting a well-respected, board certified FP in our community in the recruitment of a board prepared/certified Family Physician to be the core of a single specialty group. OB and procedures are optional. Excellent compensation and benefits available. Located in the beautiful Eastern Upper Peninsula of Michigan, Sault Ste. Marie is a mecca of both winter and summer outdoor recreation and offers a superior quality of life. For more information contact: Elsa Abner-Taschwer at 800-635-4608 or forward your CV to: War Memorial Hospital, 500 Osborn Boulevard, Sault Ste. Marie, MI 49783.

IOWA — A FAMILY PHYSICIAN'S FAMILY HAVEN — Bring your family to a safe wholesome area rich with leisure, cultural and educational opportunities. We are in need of BE/BC Family Physicians to join our growing PHO of primary care physicians. Highly competitive salary and compensation package. Practice patient-oriented medicine in a group concerned with your quality of life. Send CV to: Theresa Alberts, Recruiting Specialist, 855 A Avenue NE, Suite 100, Cedar Rapids, IA 52402. Telephone: 319-366-3400.

NORTHEASTERN WISCONSIN — Six-person FP group is recruiting BE/BC Physician. Busy practice with full range of clinical services, including OB. Comfortable community with an excellent lifestyle. Located between Green Bay and Milwaukee. Low crime. Excellent schools. Several colleges and universities nearby. Competitive salary, productivity bonus, and fringe benefits. Send CV to: Reply Box 10380, JABFP.
ACADEMIC POSITION — Join the academic team in the Department of Family and Community Medicine at the University of Illinois College of Medicine at Rockford. This nationally recognized department has an opening for a physician in an innovative ambulatory primary care setting where faculty supervise medical students in delivering health care. As students spend one day a week for 2.5 years following up to 100 families, this is the perfect opportunity to combine genuine clinical practice with effective one-on-one teaching in an academic environment. Candidates must be board certified/board eligible. A willingness to provide obstetrical care is desirable. Rank commensurate with qualifications. Scholarly time is available and beginning faculty can qualify for a new two year Faculty Development Fellowship. Innovative programs of teaching and research in rural medical education, patient-centered clinical method, international medical education and in community-based medical education are in progress. The environment for family medicine at the College of Medicine at Rockford is outstanding. Come join with us in our vision! For further discussion please contact: Ron McCord, MD, 1601 Parkway Avenue, Rockford, IL 61071-1997. 815-395-5810. The University of Illinois is an Equal Opportunity/Affirmative Action Employer.

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Southwest

OKLAHOMA — Experience the hospitality of the southwest in Oklahoma. We are interested in the addition of BC/BE family physicians to join our growing multispecialty group practice. Salary guarantee, incentive bonus and generous benefits are offered. Contact: Debbie Jones, Oklahoma City Clinic, 701 NE 10th, Oklahoma City, OK 73104. 800-522-0224, ext. 2591.

EXCELLENT OPPORTUNITIES AVAILABLE IMMEDIATELY — For BC/BE Family Practitioners to staff family practice clinics in a sunny southeast Texas community close to a large metro city and which offers an excellent quality of life and good schools. Extremely competitive first year net income guarantee with the potential for succeeding years exceptional. With these opportunities the hassle of managing an office is gone. Interview, relocation and marketing expense written. Interested applicants please forward CV to: Pat Adams, AMI Park Place Medical Center, PO Box 1648, Port Arthur, TX 77641 or fax to: 409-983-6152.

SEEKING BOARD CERTIFIED FP OR INTERNIST — To serve as Medical Director of 40+ member, non-profit primary care group. Administrative duties will include recruitment and development of outstanding practitioners, coordination of resident education activities, compensation issues, and generally building on the momentum which the group has already achieved. Must be willing to devote a substantial proportion of time to patient care and must be capable of establishing a high standard by example. Compensation negotiable. Administrative experience or training preferred. Please send CV to: Patrick Williamson, MD, Solomon Anthony Clinic, 2833 Babcock, Suite 200, San Antonio, TX 78229 or fax: 210-616-7343.

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For more information, contact your local Navy Medical Programs officer or call 1-800-USA-NAVY. Ask for operator 36.

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ACULAR® (ketorolac tromethamine) 0.5%
Sterile Ophthalmic Solution

INDICATIONS AND USAGE
ACULAR® ophthalmic solution is indicated for the relief of ocular itching due to seasonal allergic conjunctivitis.

CONTRAINDICATIONS
ACULAR® ophthalmic solution is contraindicated in patients while wearing soft contact lenses and in patients with previously demonstrated hypersensitivity to any of the ingredients in the formulation.

WARNINGS
There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory agents. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

With some nonsteroidal anti-inflammatory drugs, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that oculary applied nonsteroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

PRECAUTIONS
General: It is recommended that ACULAR® ophthalmic solution be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: An 18-month study in mice at oral doses of ketorolac tromethamine equal to the parental MRHD (Maximum Recommended Human Dose) and a 24-month study in rats at oral doses 2.5 times the parental MRHD, showed no evidence of tumorigenicity. Ketorolac tromethamine was not mutagenic in Ames test, unscheduled DNA synthesis and repair, and in forward mutation assays. Ketorolac did not cause chromosome breakage in the in vivo mouse micronucleus assay. At 1590 ug/mL (approximately 1000 times the average human plasma levels) and at higher concentrations ketorolac tromethamine increased the incidence of chromosomal aberrations in Chinese hamster ovarian cells. Impairment of fertility did not occur in male or female rats at oral doses of 9 mg/kg (33.1 mg/m²) and 16 mg/kg (54.4 mg/m²) respectively.

Pregnancy: Pregnancy Category C. Reproduction studies have been performed in rabbits, using daily oral doses at 3.6 mg/kg (42.35 mg/m²) and in rats at 10 mg/kg (59 mg/m²) during organogenesis. Results of these studies did not reveal evidence of teratogenicity to the fetus. Oral doses of ketorolac tromethamine at 1.5 mg/kg (8.8 mg/m²), which was half of the human oral exposure, administered after gestation day 17 caused dystocia and higher pup mortality in rats. There are no adequate and well-controlled studies in pregnant women. Ketorolac tromethamine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Caution should be exercised when ACULAR® is administered to a nursing woman.

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

ADVERSE REACTIONS
In patients with allergic conjunctivitis, the most frequent adverse events reported with the use of ACULAR® ophthalmic solution have been transient stinging and burning on instillation. These events were reported by approximately 40% of patients treated with ACULAR® ophthalmic solution. In all development studies conducted, other adverse events reported during treatment with ACULAR® include ocular irritation (3%), allergic reactions (3%), superficial ocular infections (0.5%) and superficial keratitis (1%).

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