ZIAC controls mild-to-moderate hypertension in up to 80% of patients\(^1\)

ZIAC controls blood pressure for a full 24 hours for true once-a-day dosing\(^2\)

ZIAC minimizes traditional beta-blocker- and HCTZ-associated metabolic effects (hypokalemia, hyperuricemia, hypercholesterolemia, hyperglycemia)\(^1\)

*The two most common side effects — dizziness and fatigue — occurred at rates comparable to placebo.

ZIAC is contraindicated in patients in cardiogenic shock, overt cardiac failure (see WARNINGS section of full Prescribing Information), second- or third-degree AV block, marked sinus bradycardia, anuria, and hypersensitivity to either component of this product or to other sulfonamide-derived drugs. Please see Brief Summary of Prescribing Information on adjacent page.
Ziac™ (Bisoprolol Fumarate and Hydrochlorothiazide) Tablets

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DESCRIPTION

Bisoprolol fumarate and hydrochlorothiazide is indicated for the treatment of hypertension. It combines two antihypertensive agents in a once-daily dosage: a selective beta1-adrenoceptor blocking agent (bisoprolol fumarate) and a benzothiazide diuretic (hydrochlorothiazide).

CLINICAL STUDIES

Bisoprolol fumarate and hydrochlorothiazide are indicated for the treatment of hypertension when used alone or in combination with other antihypertensive agents. In controlled clinical trials, the plasma half-life of bisoprolol fumarate is increased up to threefold, as compared to healthy subjects.

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, which may result in hypomagnesemia. Hypokalemia may develop. Hypokalemia may increase the risk of digoxin toxicity. In addition, hypokalemia and other electrolyte imbalances may cause cardiac arrhythmias and may exaggerate the response of the heart to the toxic effects of digitalis. Additional hypokalemia may occur in elderly patients in hot weather, particularly when given with a potassium-sparing diuretic such as spironolactone or triamterene, or when given with potassium-sparing diuretics or potassium-sparing agents such as螺内酯. Parathyroid Disease: Patients with hyperparathyroidism may be followed by an exacerbation of digitalis toxicity when given with a potassium-sparing agent. Also, latent parathyroid disease may be manifested by an exacerbation of digitalis toxicity when given with a potassium-sparing agent. Systemic: Beta-blocking agents should be avoided in patients with overt cardiac failure.

ADVERSE REACTIONS

Body System/Adverse Experience: All Adverse Reactions (% of Patients with Adverse Experiences)* Body System/Adverse Experience: Drug-related Adverse Experience: % of Patients with Adverse Experiences* Cardiovascular

- Bradycardia 0.7
- Orthostatic hypotension 0.7
- Clotting disorders 0.9
- Stroke 0.9
- Myocardial infarction 0.9

Other Laboratory Changes Included Small Increases in Uric Acid, Intrahepatic Cholestasis (cholestatic jaundice), fever, dyspepsia, nausea, vomiting, anemia, dyspnea, chest pain, pneumonia, tachycardia, angina, and hypotension can increase the metabolic clearance of digitalis glycosides, thereby decreasing digitalis toxicity.

LABORATORY ABNORMALITIES

- Decrease in the serum level of potassium and magnesium
- Hypokalemia and other electrolyte imbalances

NOTE: 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).

- Rash, bruising, pruritus, flushing, sweating, urticaria, serpiginous, dermatitis, exfoliative dermatitis (very rarely).
- Special Sensitivity: Rash, urticaria, angioedema, abnormal laceration, thrombosis, decreased hearing, thirst, taste abnormalities.

ECONOMIC IMPACT Coding:

- Cardiac: Angina, bradycardia, conduction disturbances, congestive failure, dysrhythmias, hyperkalemia, hypotension, hypotension, hypothermia, hypovolemia, metabolic acidosis, myocardial infarction, syncope, tachycardia.
- Respiratory: Bronchitis, bronchospasm, hypoxia, pneumonia, pulmonary edema, respiratory failure.
- GI: Diarrhea, dyspepsia, nausea, vomiting.
- Urinary: Hematuria, proteinuria, polyuria.
- Dermatologic: Alopecia, pruritus, skin rash.
- Miscellaneous: Fatigue, anxiety, anxiety, depression, somnolence, numbness, paresthesias, tremor.

*Adverse reactions are listed by individual body system and drug class. Adverse reactions are listed separately for each body system. Adverse reactions are listed separately for each drug class. Adverse reactions are listed separately for each individual and drug class. Adverse reactions are listed separately for each body system and drug class.

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THAT WORKS
A unique topical analgesic cream, ZOSTRIX has a mechanism of action that complements NSAIDs. NSAIDs inhibit prostaglandin synthesis, while capsaicin, the active ingredient in ZOSTRIX, depletes substance P, a neurotransmitter of pain.

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ZOSTRIX delivers pain-relieving action directly to the joint that hurts. A new clinical study shows that application of capsaicin cream reduces the levels of substance P and other biochemical mediators in the synovial fluid of arthritic joints.

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**Clinical Review.** In-depth reviews of specific clinical problems, disease entities, or treatment modalities; comprehensive and critical analysis of the literature is required (usual maximum length 5000 words).

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