Bizolol® Plus

Bisoprolol Fumarate + Hydrochlorothiazide

COMPOSITION

Bizolol® Plus 2.5/6.25 tablet: Each film coated tablet contains Bisoprolol Fumarate USP 2.5 mg and Hydrochlorothiazide BP 6.25 mg.
Bizolol® Plus 5/6.25 tablet: Each film coated tablet contains Bisoprolol Fumarate USP 5 mg and Hydrochlorothiazide BP 6.25 mg.

PHARMACOLOGY

Bisoprolol Fumarate and Hydrochlorothiazide have been used individually and in combination for the treatment of hypertension. The antihypertensive effects of these agents are additive; Hydrochlorothiazide 6.25 mg significantly increases the antihypertensive effect of Bisoprolol Fumarate. The incidence of hypokalemia with the Bisoprolol Fumarate and Hydrochlorothiazide 6.25 mg combination is significantly lower than with Hydrochlorothiazide 25 mg. Bisoprolol Fumarate is a β_1-selective (cardioselective) adrenoceptor blocking agent without significant membrane stabilizing or intrinsic sympathomimetic activities in its therapeutic dose range. Hydrochlorothiazide is a benzothiadiazine diuretic. Thiazides affect renal tubular mechanisms of electrolyte reabsorption and increase excretion of sodium and chloride in approximately equivalent amounts.

INDICATION

Management of hypertension.

DOSAGE & ADMINISTRATION

Bisoprolol is an effective treatment of hypertension in once-daily doses of 2.5 to 40 mg, while Hydrochlorothiazide is effective in doses of 12.5 to 50 mg. In clinical trials of Bisoprolol/Hydrochlorothiazide combination therapy using Bisoprolol doses of 2.5 to 20 mg and Hydrochlorothiazide doses of 6.25 to 25 mg, the antihypertensive effects increased with increasing doses of either component.

Initial Therapy

Antihypertensive therapy may be initiated with the lowest dose of **Bizolol® Plus**, one 2.5/6.25 mg tablet once daily. Subsequent titration (14 day intervals) may be carried out with **Bizolol® Plus** tablets up to the maximum recommended dose 20/12.5 mg once daily, as appropriate.

Replacement Therapy

The combination may be substituted for the titrated individual components.

Therapy Guided by Clinical Effect

A patient whose blood pressure is not adequately controlled with 2.5-20 mg Bisoprolol daily may instead be given **Bizolol® Plus**. Patients whose blood pressures are adequately controlled with 50 mg of Hydrochlorothiazide daily, but who experience significant potassium loss with this regimen, may achieve similar blood pressure control without electrolyte disturbance if they are switched to **Bizolol® Plus**.

CONTRAINDICATION

It 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.

PRECAUTION

Hyperuricemia or acute gout may be precipitated in certain patients receiving thiazide diuretics. Warning signs or symptoms of fluid and electrolyte imbalance include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastrointestinal disturbances such as nausea and vomiting. Hypokalemia may develop. If withdrawal of this combination therapy is planned, it should be achieved gradually over a period of about 2 weeks. Patients should be carefully observed.

SIDE EFFECT

Generally well tolerated. Most side e□ ects have been mild and transient. Side effects which may occur: fatigue, dizziness, headache, bradycardia, arrhythmia, peripheral ischemia, chest pain, palpitations, rhythm disturbances, cold extremities, claudication, orthostatic hypotension, diarrhoea, constipation, nausea, dyspepsia, rhinitis, pharyngitis etc.

USE IN PREGNANCY AND LACTATION

Use in Pregnancy:

Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. Bisoprolol Fumarate and Hydrochlorothiazide combination should be used during pregnancy only if the potential beneft justifies the risk to the fetus.

Use in Nursing Mothers:

Bisoprolol Fumarate alone or in combination with Hydrochlorothiazide has not been studied in nursing mothers. Thiazides are excreted in human breast milk. Small amounts of Bisoprolol Fumarate have been detected in the milk of lactating rats. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

DRUG INTERACTION

This combination drug may potentiate the action of other antihypertensive agents used concomitantly. This combination drug should not be combined with other beta-blocking agents. Patients receiving catecholamine-depleting drugs, such as reserpine or guanethidine, should be closely monitored because the added beta-adrenergic blocking action of Bisoprolol Fumarate may produce excessive reduction of sympathetic activity. In patients receiving concurrent therapy with clonidine, if therapy is to be discontinued, it is suggested that this combination drug be discontinued for several days before the withdrawal of clonidine. This combination drug should be used with caution when myocardial depressants or inhibitors of AV conduction, such as certain calcium antagonists (particularly of the phenylalkylamine [verapamil] and benzothiazepine [diltiazem] classes), or antiarrhythmic agents, such as disopyramide, are used concurrently. Both digitalis glycosides and beta-blockers slow atrioventricular conduction and decrease heart rate. Concomitant use can increase the risk of bradycardia.

OVERDOSE

There are limited data on overdose with this combination product. The most frequently observed signs expected with overdosage of a beta-blocker are bradycardia and hypotension. Lethargy is also common and with severe overdoses, delirium, coma, convulsions and respiratory arrest have been reported to occur. Congestive heart failure, bronchospasm and hypoglycemia may occur. With thiazide diuretics, acute intoxication is rare. The most prominent feature of overdose is acute loss of fluid and electrolytes. Signs and symptoms include cardiovascular (tachycardia, hypotension, shock), neuromuscular (weakness, confusion, dizziness, cramps of the calf muscles, paresthesia, fatigue, impairment of consciousness), gastrointestinal (nausea, vomiting, thirst), renal (polyuria, oliguria or anuria), and laboratory findings (hypokalemia, hyponatremia, hypochloremia, alkalosis, increased BUN [especially in patients with renal insufficiency]).

STORAGE CONDITION

Store below 30°C in dry place. Keep away from light.
Keep out of reach of children.

HOW SUPPLIED

Bizolol® Plus 2.5/6.25 tablet: Each box contains 10 / 30 / 60 tablets in blister pack.
Bizolol® Plus 5/6.25 tablet: Each box contains 10 / 30 / 60 tablets in blister pack.

SQUARE