Tenobis Plus
Tablet

DRUG INTERNATIONAL LTD.

Composition : **Tenobis Plus 2.5 :** Each film coated tablet contains Bisoprolol Fumarate USP 2.5 mg & Hydrochlorothiazide USP 6.25 mg.

Tenobis Plus 5 : Each film coated tablet contains Bisoprolol Fumarate USP 5 mg & Hydrochlorothiazide USP 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 β1-selective (cardioselective) adrenoceptor blocking agent without significant membrane stabilizing or intrinsic sympathomimetic activities in its therapeutic dose range.

Indications : It is indicated in the management of hypertension.

Dosage and 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 **Tenobis Plus** 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 one 2.5/6.25 mg tablet once daily. Subsequent titration (14 day intervals) may be carried out with **Tenobis Plus** 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 **Tenobis Plus**. Patients whose blood pressures are adequately controlled with 50mg 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 **Tenobis Plus**. Or, as directed by the registered physician.

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.

Precautions : 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 effects : Generally well tolerated. Most side effects 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, diarrhea, constipation, nausea, dyspepsia, rhinitis, pharyngitis etc.

Use in Pregnancy and lactation : **Pregnancy Category C :** There are no adequated and well-controlled studies in pregnant women. Bisoprolol fumarate and hydrochlorothiazide combination should be used during pregnancy only if the potential benefit justifies the risk to the fetus. **Nursing mothers :** Bisoprolol fumarate alone or in combination with HCTZ 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 in to account the importance of the drug to the mother.

Use in Child : There is no data available.

Drug Interactions : 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.

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.

Storage : Store below 30°C in a dry place.

Packing : **Tenobis Plus 2.5 :** Each box contains 2 x 14's tablets in blister pack.

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