Noxidil

COMPOSITION

Each tablet contains

Minoxidil	5 mg
Minoxidil	10 mg

DESCRIPTION

Noxidil tablet

White round biconvex tablets with a breakline on one side and the figure "5" on the other.

Noxidil Forte Tablet

White round biconvex tablets with a breakline on one side and the figure "10" on the other.

PHARMACOLOGY

Minoxidil is an orally effective direct acting peripheral vasodilator that reduces elevated systolic and diastolic blood pressure by decreasing peripheral vascular resistance. Microcirculatory blood flow in animals is enhanced or maintained in all systemic vascular beds. In man, forearm and renal vascular resistance decline; forearm blood flow increases while renal blood flow and glomerular filtration rate are preserved.

Because it causes peripheral vasodilation, minoxidil elicits a number of predictable reactions. Reduction of peripheral arteriolar resistance and the associated fall in blood pressure trigger sympathetic, vagal inhibitory, and renal homeostatic mechanisms, including an increase in renin secretion, that lead to increased cardiac rate and output and salt and water retention. These adverse effects can usually be minimized by concomitant administration of a diuretic and a beta-adrenergic blocking agent or other sympathetic nervous system suppressant.

Minoxidil does not interfere with vasomotor reflexes and therefore does not produce orthostatic hypotension. The drug does not enter the central nervous system in experimental animals in significant amounts, and it does not affect CNS function in man.

PHARMACOKINETICS

Absorption and Metabolism

Minoxidil is at least 90% absorbed from the GI tract in experimental animals and man. Plasma levels of the parent drug reach maximum within the first hour and decline rapidly thereafter. The average plasma half-life in man is 4.2 hours. Approximately 90% of the administered drug is metabolized, predominantly by conjugation with glucuronic acid at the N-oxide position in the pyrimidine ring, but also by conversion to more polar products. Known metabolites exert much less pharmacologic effect than minoxidil itself; all are excreted principally in the urine. Minoxidil does not bind to plasma proteins, and its renal clearance corresponds to the glomerular filtration rate. In the absence of functional renal tissue, minoxidil and its metabolites can be removed by hemodialysis.

INDICATIONS

Treatment of severe hypertension

DOSAGE AND ADMINISTRATION

Patients over 12 years of age

The recommended initial dosage is 5 mg of minoxidil given as a single daily dose. Daily dosage can be increased to 10, 20 and then to 40 mg in single or divided doses if required for optimum blood pressure control. The effective dosage range is usually 10 to 40 mg per day. The maximum recommended dosage is 100 mg per day.

Patients under 12 years of age

The initial dosage is 0.2 mg/kg minoxidil as a single daily dose. The dosage may be increased in 50 to 100% increments until optimum blood pressure control is achieved. The effective dosage range is usually 0.25 to 1.0 mg/kg/day. The maximum recommended dosage is 50 mg daily

Frequency of dosage adjustment

Dosage must be titrated carefully according to individual response. Intervals between dosage adjustments normally should be at least 3 days since the full response to a given dose is not obtained for at least that amount of time.

CONTRAINDICATION

Minoxidil Tablets are contraindicated in pheochromocytoma, because it may stimulate secretion of catecholamines from the tumor through its antihypertensive action. Minoxidil is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTION AND WARNING

For hypertension, minoxidil must usually be administered with a diuretic to prevent fluid retention; a loop diuretic is almost always required. Drugs or regimens that provide around the clock sympathetic suppression are usually required to prevent tachycardia, which can precipitate or worsen existing angina. Degenerative myocardial lesions reported in animal studies have yet to be confirmed in humans.

DRUG INTERACTIONS

Concomitant therapy with guanethidine can result in profound orthostatic hypotension; discontinue guanethidine 1-3 weeks before initiation of oral minoxidil therapy or initiate therapy in the hospital

PREGNANCY AND LACTATION

Although there are no adequate and controlled studies to date in humans receiving oral or topical minoxidil, orally administered minoxidil has been associated with evidence of increased fetal resorption in rabbits, but not rats, when given at dosage 5 times the maximum recommended human oral antihypertensive dosage. There was no evidence of teratogenic effects of orally administered minoxidil in rats or rabbits.

There has been one report of minoxidil excretion in the breast milk of a woman treated with 5 mg oral minoxidil twice daily for hypertension. Because of the potential for adverse effects in nursing infants from minoxidil absorption, so minoxidil should not be administered to a nursing woman.

ADVERSE EFFECTS

Frequently, hypertrichosis (elongation, thickening and enhanced pigmentation) (80%), transient ECG T-wave changes (60%), temporary edema (7%), or tachycardia occurs. Occasionally, pericardial effusion with or without tamponade (3%), CHF or angina occurs. Rarely, breast tenderness and rashes (including Stevens-Johnson syndrome) occur. Minor dermatologic reactions occur occasionally after topical application

OVERDOSAGE

There have been only a few instances of deliberate or accidental overdosage with Minoxidil Tablets. One patient recovered after taking 50 mg of minoxidil together with 500 mg of a barbiturate. When exaggerated hypotension is encountered, it is most likely to occur in association with residual sympathetic nervous system blockade from previous therapy (guanethidine-like effects or alpha-adrenergic blockage), which prevents the usual compensatory maintenance of blood pressure. Intravenous administration of normal saline will help to maintain blood pressure and facilitate urine formation in these patients. Sympathomimetic drugs such as norepinephrine or epinephrine should be avoided because of their excessive cardiac stimulating action. Phenylephrine, angiotensin II, vasopressin, and dopamine all reverse hypotension due to Minoxidil, but should only be used if underperfusion of a vital organ is evident.

Manufactured by

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