MINISON TABLET 1MG

Prazosin Hydrochloride is an α-adrenoreceptor blocking drug used in the treatment of hypertension. Chemically, it is designated 1-(4-Amino-6, 7-dimethoxy-2-quinazolinyl) -4-(2-furanylcarbonyl) piperazine hydrochloride.

Ingredient(s)
Each tablet contains:
Prazosin Hydrochloride 1.095mg
(eq. to Prazosin ..... 1mg)

Pharmacodynamic:
Prazosin, an antihypertensive agent, is thought to act by selective blockade of alpha$_1$ – adrenoreceptors producing peripheral dilatation of both arterioles and veins and reduction of peripheral resistance, usually without reflex tachycardia.

Prazosin reduces both preload and afterload and produces an improvement in cardiac output in patients with congestive heart failure.

Prazosin hydrochloride causes a decrease in total peripheral vascular resistance. Animal studies suggest that the vasodilator effect of prazosin hydrochloride is related to blockade of post-synaptic alpha-1-adrenoceptors. The results of forearm plethysmographic studies in humans demonstrate that the peripheral vasodilation is a balanced effect on both resistance vessels (arterioles) and capacitance vessels (veins).

Unlike non-selective alpha-adrenergic blocking agents, the antihypertensive action of prazosin hydrochloride is usually not accompanied by reflex tachycardia.

Most studies indicate that chronic therapy with prazosin hydrochloride has little effect on plasma renin activity. One report suggests a transient increase in plasma renin activity following the initial dose, as well as an attenuated, transient increase with subsequent doses.

Hemodynamic studies have been carried out in hypertensive patients following single dose administration and during the course of long-term maintenance therapy. The results confirm that the usual therapeutic effect is a fall in blood pressure unaccompanied by a clinically significant change in cardiac output, heart rate, renal blood flow, or glomerular filtration rate. Clinically, the antihypertensive effect is believed to be a direct result of peripheral vasodilation. In humans, blood pressure is lowered in both the supine and standing positions. This effect is more pronounced on the diastolic blood pressure. Tolerance has not been observed in long-term clinical use. Rebound elevation of blood pressure does not occur following abrupt cessation of therapy with prazosin hydrochloride.

A variety of epidemiologic, biochemical and experimental studies have established that an elevated level of low-density lipoprotein (LDL) cholesterol is associated with an increased risk of coronary heart disease. There is an even stronger relationship between reduced levels of high-density lipoprotein (HDL) cholesterol and an increased risk of coronary heart disease. Clinical studies have shown that prazosin hydrochloride lowers LDL levels and either has no effect or increases HDL levels.

Pharmacokinetics:
Following oral administration in normal volunteers and hypertensive patients, plasma concentrations reach a peak in 1 to 2 hours, with a plasma half-life of 2 to 3 hours. Pharmacokinetic data in a limited number of patients with left ventricular failure, most of whom showed evidence of hepatic congestion, indicate that peak plasma concentrations are reached in 2.5 hours and plasma half-life is approximately 7 hours. The drug is highly bound to plasma protein. Animal studies indicate that prazosin hydrochloride is extensively metabolized, primarily by demethylation and conjugation, and excreted mainly via the bile and feces. Similar metabolism and excretion have been documented in human studies.

Indication(s):
Prazosin is indicated for the treatment of hypertension.

Dosage and Administration:
Hypertension
For maximum benefit, small increases should be continued until the desired effect is achieved or a total daily dosage of 20mg is reached. A diuretic or beta-adrenergic blocking agent may be added to enhance efficacy. The maintenance dosage of prazosin hydrochloride may be given as a twice- or three-times daily regimen.

A. Patients Receiving No Antihypertensive Therapy
It is recommended that therapy be initiated with 0.5mg given at bedtime, then 0.5mg two or three times daily for 3 to 7 days. Unless poor toleration suggests that the patient is unusually sensitive, this dosage should be increased to 1mg given two or three times daily for a further 3 to 7 days. Thereafter, as determined by the patient's response to the blood pressure lowering effect, the dosage should be increased gradually to a maximum total daily dosage of 20mg given in divided doses.

B. Patients Receiving Diuretic Therapy with Inadequate Control of Blood Pressure
The diuretic should be reduced to a maintenance dosage level for the particular agent, and prazosin hydrochloride should be initiated with 0.5mg at bedtime, then proceeding to 0.5mg two or three times daily.
After the initial period of observation, the dosage for prazosin hydrochloride should be gradually increased as determined by the patient's response.

C. Patients Receiving Other Antihypertensive Therapy but with Inadequate Control
Because some additive effect is anticipated, the dosage level of other agents (e.g. beta-adrenergic blocking agents, methyldopa, reserpine, clonidine, etc.) should be reduced and prazosin hydrochloride initiated at 0.5mg at bedtime then proceeding to 0.5mg two or three times daily. Subsequent dosage increase should be made depending upon the patient's response.
There is evidence that adding prazosin hydrochloride to a beta-adrenergic blocking agent, calcium antagonists or angiotensin-converting enzyme (ACE) inhibitors may bring about a substantial reduction in blood pressure. Thus, the low initial dosage regimen is strongly recommended.

D. Patients with Moderate to Severe Grades of Renal Impairment
Evidence to date shows that prazosin hydrochloride does not further compromise renal function when used in patients with renal impairment. Because some patients in this category have responded to small doses of prazosin hydrochloride, it is recommended that therapy be initiated at 0.5mg daily and that dosage increases be instituted with caution.

Route of Administration:
Oral.

Contraindication(s):
Hypersensitivity to any component of this drug or quinazolines.

Precaution(s) / Warning(s):
1. A very small percentage of patients have responded in an abrupt and exaggerated manner to the initial dose of prazosin hydrochloride. Postural hypotension evidenced by dizziness and weakness, or rarely loss of consciousness, has been reported, particularly with the commencement of therapy, but this effect is readily avoided by initiating treatment with a low dose of prazosin hydrochloride and with small increases in dosage during the first 1 to 2 weeks of therapy.
2. Prazosin should be used with caution in patients with angina, and the dosage should be reduced in patients with renal failure of hepatic failure and in elderly.
3. Prazosin may cause drowsiness or dizziness; patients should be cautioned to avoid situations or activities (e.g. driving or operate machinery) where injury could result, should dizziness or weakness occur during the initiation of prazosin hydrochloride therapy.
4. As with other alpha-1 blockers, concomitant administration of prazosin hydrochloride with a phosphodiesterase type-5 (PDE-5) inhibitor should be used with caution, as it may lead to symptomatic hypotension in some patients. No studies have been conducted with prazosin hydrochloride.
5. Safe use of this product during pregnancy has not been established. The product should be given to women who suspect pregnancy or to pregnant women only when clearly needed. Prazosin has been shown to be excreted in small amount in human milk. Caution should be exercised when Prazosin is administered to nursing mothers.
6. Children: Not recommended for children under 12 years.

Interactions with Other Medicaments:
Prazosin hydrochloride has been administered without any adverse drug interaction in clinical experience to date with the following:
1) Cardiac glycosides: digitalis and digoxin
2) Hypoglycaemic agents: insulin, chlorpropamide, phenformin, tolazamide and tolbutamide
3) Tranquilizers and sedatives: chlordiazepoxide, diazepam and phenobarbital
4) Agents for the treatment of gout: allopurinol, colchicine and probenecid
5) Antiarrhythmic agents: procainamide, propranolol and quinidine
6) Analgesics, antipyretics and anti-inflammatory agents: propoxyphene, aspirin, indomethacin and phenylbutazone type.

Additional of a diuretic or other antihypertensive agent to prazosin hydrochloride has been shown to cause an additive hypotensive effect. This effect can be minimized by reducing the dose of prazosin hydrochloride to 1mg to 2mg three times a day, by introducing additional antihypertensive drugs cautiously and then by retitrating prazosin hydrochloride based on clinical response.

False-positive results may occur in screening tests for pheochromocytoma (urinary vanillylmandelic acid [VMA] and methoxyhydroxyphenylglycol [MHPG], urinary metabolites of norepinephrine) in patients who are being treated with prazosin hydrochloride.

In clinical studies in which lipid profiles were followed, there were generally no adverse changes noted between pre- and post-treatment lipid levels.
Side Effect(s) / Adverse Reaction(s):
The most common reactions associated with prazosin hydrochloride therapy are:

Body as a Whole	Lack of energy, weakness (asthenia)
Central & Peripheral Nervous	Dizziness (faintness), headache
Gastrointestinal	Nausea
Heart Rate/ Rhythm	Palpitations
Psychiatric	Drowsiness

In most instances side effects have disappeared with continued therapy or have been tolerated with no decrease in dosage of the drug.

In additional, the following reactions have been associated with prazosin hydrochloride therapy:

Autonomic Nervous	Diaphoresis, dry mouth, flushing, priapism
Body as a Whole	Allergic reaction, asthenia (weakness), fever, malaise, pain
Cardiovascular, General	Angina pectoris, edema, hypotension, orthostatic hypotension, syncope
Central & Peripheral Nervous	Faintness (dizziness), paresthesia, vertigo
Collagen	Positive ANA titer
Endocrine	Gynecomastia
Gastrointestinal	Abdominal discomfort and/or pain, constipation, diarrhea, pancreatitis, vomiting
Hearing/Vestibular	Tinnitus
Heart Rate/ Rhythm	Bradycardia, tachycardia
Liver/ Biliary	Liver function abnormalities
Musculoskeletal	Arthralgia
Psychiatric	Depression, hallucinations, impotence, insomnia, nervousness
Respiratory	Dyspnea, epistaxis, nasal congestion
Skin & Appendages	Alopecia, pruritus, rash, lichen planus, urticaria
Urinary	Incontinence, urinary frequency
Vascular (Extracardiac)	Vasculitis
Vision	Blurred vision, reddened sclera, eye pain

Some of these reactions have occurred rarely, and in many instances the exact causal relationships have not been established. Literature reports exists associating prazosin hydrochloride therapy with a worsening of pre-existing narcolepsy. A causal relationship is uncertain in these cases.

Symptoms and Treatment for Overdosage, and Antidote(s):
Should overdosage lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplish by keeping the patient in a supine position. If this measure is inadequate, shock should be first treated with volume expanders. If necessary, vasopressors should then be used. Renal function should be monitored and supported as needed. Laboratory data indicate Prazosin is not dialyzable because it is protein bound.

Shelf- Life:
3 years from the date of manufacture.

Storage Condition(s):
Keep in a tight container. Store at temperature below 30ºC. Protect from light and moisture.

Product Description & Packing(s):
A light salmon color elliptical tablet with one side scored.
The tablet can be divided into equal halves.
List of excipients:
Lactose Monohydrate, Potato Starch, Sunset Yellow *(sunset yellow FCF Aluminium Lake)*, Sodium Starch Glycolate, Talc, Magnesium Stearate, Magnesium Aluminometasilicate and Purified Water.
Plastic bottle of 250's.
Plastic bottle of 500's and 1000's(for export only).
Blister packing of 10's x 50.
Not all presentation may be available locally.

Y. S. P.®

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