160 mm

240 mm

Please read carefully!

T.O. PRAZOSIN 1 MG & T.O. PRAZOSIN 2 MG TABLET

DESCRIPTION
T.O. Prazosin 1 mg Tablet: An orange, round biconvex tablet with a breakline on one side. Each tablet contains prazosin hydrochloride (HCl) 1.095 mg (equivalent to prazosin 1 mg).
T.O. Prazosin 2 mg Tablet: A white, round biconvex tablet with a breakline and a figure "2"on one side and the letters "TOC"on the other. Each tablet contains prazosin hydrochloride (HCl) 2.190 mg (equivalent to prazosin 2 mg).

PHARMACODYNAMICS
Pharmacotherapeutic group: Alpha-adrenoreceptor antagonists
ATC code: C02CA01
Prazosin hydrochloride causes a decrease in total peripheral vascular resistance through selective inhibition of postsynaptic alpha-1-adrenoreceptors in vascular smooth muscle. The results of forearm plethysmographic studies in humans demonstrate that the resultant peripheral vasodilatation is a balanced effect on both resistance vessels (arterioles) and capacitance vessels (veins).
In hypertensive patients, blood pressure is lowered in both the supine and standing positions; this effect is more pronounced on the diastolic blood pressure. Tolerance to the antihypertensive effect has not been observed in long-term clinical use; relatively little tachycardia or change in renin levels has been noted. Rebound elevation of blood pressure does not occur following abrupt cessation of prazosin hydrochloride therapy.
The therapeutic efficacy of prazosin hydrochloride in patients with congestive heart failure is ascribed to a reduction in left ventricular filling pressure, reduction in cardiac impedance and an augmentation of cardiac output. The use of prazosin hydrochloride in congestive heart failure does not provoke a reflex tachycardia and blood pressure reduction is minimal in normotensive patients. Prazosin hydrochloride has been found to successfully reduce the severity of the signs, symptoms, frequency, and duration of attacks, in patients with Raynaud's disease.
In low dosage, antagonism of alpha-1-receptors on prostatic and urethral smooth muscle has been shown to improve the urinary pressure profile in men and to improve symptoms of benign prostatic hypertrophy. Clinical studies have shown that prazosin hydrochloride therapy is not associated with adverse changes in the serum lipid profile.

PHARMACOKINETICS
Absorption
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.
Metabolism
The drug is highly bound to plasma protein. Studies reported indicate that prazosin hydrochloride is extensively metabolised, primarily by demethylation and conjugation.
Excretion
Prazosin hydrochloride is excreted mainly via bile and faeces.

INDICATIONS
Hypertension
T.O. Prazosin 1 mg / 2 mg Tablet is indicated in the treatment of all grades of essential (primary) hypertension and all grades of secondary hypertension of varied aetiology. It can be used as the initial and sole agent or it may be employed in a treatment program in conjunction with a diuretic and/or other antihypertensive drugs, as needed, for proper patient response.
Left Ventricular Failure
T.O. Prazosin 1 mg / 2 mg Tablet is indicated in the treatment of left ventricular failure. Prazosin hydrochloride may be added to the therapeutic regimen in patients who have not shown a satisfactory response or who have become refractory to conventional therapy with diuretics, with or without cardiac glycosides.
Benign Prostatic Hyperplasia
T.O. Prazosin 1 mg / 2 mg Tablet is indicated as an adjunct in the symptomatic treatment of urinary obstruction caused by benign prostatic hyperplasia (BPH). It is also of value in patients awaiting prostatic surgery.
Raynaud's Phenomenon and Raynaud's Disease
T.O. Prazosin 1 mg / 2 mg Tablet is indicated in the treatment of Raynaud's phenomenon and Raynaud's disease.

RECOMMENDED DOSAGE
T.O. Prazosin 1 mg / 2 mg Tablet is administered orally.
There is evidence that toleration is best when therapy is initiated with a low starting dose of prazosin hydrochloride. During the first week, the dosage of prazosin hydrochloride should be adjusted according to the patient's individual toleration. Thereafter, the daily dosage is to be adjusted on the basis of the patient's response.. Response is usually seen within 1 to 14 days if it is to occur at any particular dose. When a response is seen, therapy should be continued at that dosage until the degree of response has reached the optimum before the next dose increment is added.
Hypertension
For maximum benefit, small increases should be continued until the desired effect is achieved or a total daily dosage of 20 mg 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 0.5 mg given at bedtime, then 0.5 mg 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 1 mg 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 20 mg 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 0.5 mg at bedtime, then proceeding to 0.5 mg 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 Antihypertensives 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 0.5 mg at bedtime, then proceeding to 0.5 mg 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 0.5 mg daily and that dosage increases be instituted with caution.
Left Ventricular Failure
The recommended starting dose is 0.5 mg two, three or four times a day. Dosage should be titrated according to the patient's clinical response, based on careful monitoring of cardiopulmonary signs and symptoms, and when indicated, hemodynamic studies. Dosage titration steps may be performed as often as every 2 or 3 days in patients under close medical supervision. In severely ill, decompensated patients, rapid dosage titration over 1 to 2 days may be indicated, and is best done when hemodynamic monitoring is available. In published clinical studies, the therapeutic dosages ranged from 4 mg to 20 mg daily in divided doses. Adjustment of dosage may be required in the course of prazosin hydrochloride therapy in some patients to maintain optimal clinical improvement.
Benign Prostatic Hyperplasia
The recommended starting dose is 0.5 mg twice daily given for a period of 3 to 7 days and should then be adjusted according to the patient's clinical response. The usual maintenance dose is 2 mg twice daily. The safety and efficacy of a total daily dosage greater than 4 mg has not been established. Therefore, total daily dosages greater than 4 mg should be used with caution.
Raynaud's Phenomenon and Raynaud's Disease
The recommended starting dosage is 0.5 mg twice daily given for a period of 3 to 7 days and should be adjusted according to the patient's clinical response. The usual daily maintenance dosage is 1 mg or 2 mg twice daily. Doses up to 2 mg three times a day may be required for some patients.
Use in Children
Prazosin hydrochloride is not recommended for the treatment of children under the age of 12 years, since safe conditions for its use have not been established.

CONTRAINDICATION
T.O. Prazosin 1 mg / 2 mg Tablet is contraindicated in patients with known sensitivity to quinazolines, prazosin hydrochloride, or any of the inert ingredients.

WARNINGS AND PRECAUTIONS
Left Ventricular Failure
Prazosin hydrochloride is not recommended in the treatment of left ventricular failure due to mechanical obstruction, such as aortic valve stenosis, mitral valve stenosis, pulmonary embolism, and restrictive pericardial disease. Adequate data are not yet available to establish efficacy in patients with left ventricular failure due to a recent myocardial infarction. When prazosin hydrochloride is initially administered to patients with left ventricular failure who have undergone vigorous diuretic or other vasodilator treatment, particularly in higher than the recommended starting dose, the resultant decrease in left ventricular filling pressure may be associated with a significant fall in cardiac output and systemic blood pressure. In such patients, observance of the recommended starting dose of prazosin hydrochloride followed by gradual titration is particularly important. Occasionally, in patients with left ventricular failure, the clinical efficacy of prazosin hydrochloride has been reported to diminish after several months of treatment. In these patients, there is usually evidence of weight gain or peripheral oedema, indicating fluid retention. Since spontaneous deterioration may occur in such severely ill patients, a causal relationship to prazosin hydrochloride therapy has not been established. Thus, as with all patients with left ventricular failure, careful adjustment of diuretic dosage according to the patient's clinical condition is required to prevent excessive fluid retention and consequent relief of symptoms. In those patients without evidence of fluid retention, when clinical improvement has diminished, an increase in the dosage of prazosin hydrochloride will usually restore clinical efficacy.

160 mm

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Hypertension
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. The effect, when observed, is not related to the severity of hypertension is self-limiting and, in most patients, does not recur after the initial period of therapy or during subsequent dose-titration steps. When instituting therapy with any effective antihypertensive agent, the patient should be advised how to avoid symptoms resulting from postural hypotension and what measures to take should they develop. The patient should be cautioned to avoid situations where injury could result, should dizziness or weakness occur during the initiation of prazosin hydrochloride therapy.
Benign Prostatic Hyperplasia
Prazosin hydrochloride decreases peripheral vascular resistance, and since many patients with this disorder are elderly, careful monitoring of blood pressure during initial administration and during adjustment of the dose of prazosin hydrochloride is suggested. Close observation is especially recommended for patients taking medications that are known to lower blood pressure.
Raynaud's Phenomenon and Raynaud's Disease
Because prazosin hydrochloride decreases peripheral vascular resistance, careful monitoring of blood pressure during initial administration and titration of prazosin hydrochloride is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure.
Use with Phosphodiesterase Type-5 Inhibitors
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.
Priapism
Prolonged erections and priapism have been reported with alpha-1 blockers including prazosin hydrochloride in post-marketing experience. In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency could result.

DRUG INTERACTIONS
Addition of a diuretic or other antihypertensive agent to prazosin hydrochloride has been shown to cause an additive hypotensive effect.
There is evidence that adding prazosin hydrochloride to beta-adrenergic antagonist or calcium antagonist therapy may produce a substantial reduction in blood pressure. Therefore, the low initial dosage regimen is recommended.
Concomitant use of PDE-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil) and prazosin hydrochloride may lead to symptomatic hypotension in some patients.
Laboratory test: Patients treated with prazosin hydrochloride may provide false positive results in screening tests for phaeochromocytoma such as presenting urinary vanillylmandelic acid (VMA) and methoxyhydroxyphenyl glycol (MHPG) (a urinary metabolite of noradrenaline).

PREGNANCY AND LACTATION
Pregnancy
The safety for use of prazosin hydrochloride during pregnancy has not been established.
T.O. Prazosin 1 mg / 2 mg Tablet should only be used when clearly needed and when the potential benefits outweigh the unknown potential hazards to the foetus.
Lactation
Prazosin hydrochloride has been shown to be excreted in small amounts in human milk. **T.O. Prazosin 1 mg / 2 mg Tablet** should be used with caution in nursing mothers.

SIDE EFFECTS
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 addition, the following reactions are 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, oedema, 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 exist associating prazosin hydrochloride therapy with a worsening of pre-existing narcolepsy. A causal relationship is uncertain in these cases.
The following have been observed in patients being managed for left ventricular failure with prazosin hydrochloride when used in conjunction with cardiac glycosides and diuretics:
Autonomic Nervous: dry mouth.
Cardiovascular, General: oedema, postural hypotension.
Central & Peripheral Nervous: dizziness, headache.
Gastrointestinal: diarrhea, nausea.
Heart Rate/Rhythm: palpitations.
Psychiatric: drowsiness, impotence.
Respiratory: nasal congestion.
Vision: blurred vision.
In most instances these occurrences have been mild to moderate in severity and have resolved with continued therapy or have been tolerated with no decrease in drug dosage. The most commonly although infrequently reported side effect in the treatment of Raynaud's Phenomenon/Disease was mild dizziness.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
When instituting therapy with an effective antihypertensive agent, the patient should be advised on how to avoid symptoms resulting from postural hypotension and what measures to take should they develop.
The patient should be cautioned to avoid situation where injury could result should dizziness or weakness occur during the initiation of prazosin hydrochloride therapy (i.e. driving or operating machinery).

OVERDOSAGE
Symptoms: The symptoms reported for overdosage of prazosin hydrochloride include profound drowsiness and depressed reflexes.
Treatment: Should overdosage lead to hypotension, support of cardiovascular system is of first importance.
The patient should be placed in the supine position in order to facilitate the restoration of blood pressure and normalisation of heart rate. If this measure is inadequate, shock should first be treated with volume expanders. If necessary, vasopressors should then be used. Renal function should be monitored and supported as needed. Prazosin hydrochloride is not removed by dialysis due to the high degree of protein binding.

PACK SIZES
Blister of Alu-PVC of 10 tablets per strip. Box of 10 & 25 strips.

STORAGE CONDITIONS
Do not store above 30°C. Protect from light.
Keep out of the reach of children.
Jauhi daripada kanak-kanak.

SHELF LIFE
Please refer to the outer box label.

PRODUCT REGISTRATION HOLDER
GOODSCIENCE SDN BHD
No. 7, Jalan KPK 4/3, Kawasan Perindustrian Kundang,
Kundang Jaya, 48020 Rawang,
Selangor, Malaysia.

NAME & ADDRESS OF MANUFACTURERS
Packed and released by:
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Manufactured by:
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