DOXAZOSIN
(Doxazosin Tablets USP 4 mg)

COMPOSITION:
Each uncoated tablet contains:
Doxazosin Mesylate USP
equivalent to Doxazosin.....4 mg
Excipients q.s.

PHARMACODYNAMIC:
Pharmacotherapeutic group: Alpha-adrenoceptor antagonists
ATC code: C02CA04

Mechanism of actions:
Doxazosin is a selective and competitive antagonist of postsynaptic alpha-1-adrenergic receptors.
The administration of doxazosin causes a significant reduction in blood pressure due to decreased pheripheral vascular resistance. One daily dosage results in a clinically significant reduction in blood pressure, which will continue for 24 hours. After administration, a gradual reduction in blood pressure occurs; orthostatic effects at the start of treatment may occur. The largest decrease in blood pressure is obtained approximately 2 to 6 hours after administration

PHARMACOKINETIC:
Absoption:
Following oral administration, doxazosin is well absorbed. The peak plasma levels are achieved after 2 hours, and the absolute bioavailability is approximately 63%.

Biotransformation/Elimination:
Doxazosin is highly protein-bound in plasma (approximately 98%). The plasma-elimination occurs in two phases. The terminal half-life is 16 - 30 hours thus making the drug suitable for once daily administration. Doxazosin is predominantly metabolized by the liver and is mainly excreted by the faeces (63 - 65%); less than 5% of the dose is excreted as unchanged doxazosin. 6-Hydroxy-doxazosin is a strong and selective alpha-adrenergic receptor-blocking substance and in humans 5% of the oral dose is metabolized in this substance.
Pharmacokinetic studies in elderly and patients with renal insufficiency did not show significant pharmacokinetic differences compared to patients with a normal renal function. There are only limited data concerning the use of doxazosin in patients with liver impairment and concerning the effects of drugs known to influence hepatic metabolism (e.g. cimetidine). In a clinical study in 12 patients with mild hepatic insufficiency, single oral dose administration of doxazosin resulted in an increase in the area under the concentration-time-curve (AUC) of 43% and a decrease in clearance of 40%.

INDICATION:
Essential hypertension. Doxazosin is not appropriate for first-line treatment. It may be used as a monotherapy in patients who have failed to respond to or have contraindications to other agents. Alternatively, use should be limited to second or third line treatment in combination with other antihypertensives.
Symptomatic treatment of benign prostatic hyperplasia.

POSOLOGY AND METHOD OF ADMINISTRATION:
Method of administration:
The tablets should be administered once daily with a sufficient amount of water. The duration of treatment should be established by a physician.
Posology:
Hypertension:
Doxazosin is used in a once daily regimen: the initial dose is 1mg, to minimise the potential for postural hypotension and/or syncope (see section 4.4). Dosage may then be increased to 2mg after an additional one or two weeks of therapy and thereafter, if necessary to 4mg. The majority of patients who respond to Doxazosin will do so at a dose of 4mg or less. Dosage can be further increased if necessary to 8mg or the maximum recommended dose of 16mg.
Benign Prostatic Hyperplasia:
The recommended initial dosage of Doxazosin is 1mg given once daily to minimise the potential for postural hypotension and/or syncope (see section 4.4). Depending on the individual patient's urodynamics and BPH symptomatology dosage may then be increased to 2mg and thereafter to 4mg and up to the maximum recommended dose of 8mg. The recommended titration interval is 1-2 weeks. The usual recommended dose is 2-4mg daily.
Use in elderly:
Same dosage as for adults.
Use in patients with renal impairment:
There is no change in pharmacokinetics of doxazosin in patients with renal impairment. Therefore, the usual dose is generally recommended. Due to possible hypersensitivity in some of these patients, it may be necessary to take special care at the beginning of treatment. Doxazosin is not dialysable due to the fact that it is highly protein-bound.
Use in patients with hepatic impairment:
The dosage should be increased with special care in patients with hepatic impairment. There is no clinical experience with patients with severe hepatic impairment (see section 4.4).
Paediatric population:
'The safety and efficacy of Doxazosin in children and adolescents have not been established

SPECIAL WARNING AND PRECAUTION FOR USE:
In relation with the alpha-blocking properties of doxazosin, patients may experience postural hypotension evidenced by dizziness and weakness, or rarely loss of consciousness (syncope), particularly with the commencement of therapy. Therefore, it is prudent medical practice to monitor blood pressure on initiation of therapy to minimize the potential for postural effects. The patient should be cautioned to avoid situations where injury could result should dizziness or weakness occur during the initiation of doxazosin therapy.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency of glucose-galactose malabsorption should not take this medicine.

CONTRAINDICATION:
Hypersensitivity to the active substance or to any of the excipients.
Severe hepatic impairment.
Active pathological bleeding such as peptic ulcer or intracranial haemorrhage.

INTERACTION WITH OTHER MEDICINE AND CONCOMITANT USE:
Concomitant administration of doxazosin with a PDE-5 inhibitor may lead to symptomatic hypotension in some patients

Most (98%) of plasma doxazosin is protein bound. *In vitro* data in human plasma indicate that doxazosin has no effect on protein binding of digoxin, warfarin, phenytoin or indomethacin. Conventional doxazosin has been administered without any adverse drug interaction in clinical experience with thiazide diuretics, furosemide, beta-blockers, non-steroidal anti-inflammatory drugs, antibiotics, oral hypoglycaemic drugs, uricosuric agents, and anticoagulants. However, data from formal drug/drug interaction studies are not present.
Doxazosin potentiates the blood pressure lowering activity of other alpha-blockers and other antihypertensives.
In an open-label, randomized, placebo-controlled trial in 22 healthy male volunteers, the administration of a single 1 mg dose of doxazosin on day 1 of a four-day regimen of oral cimetidine (400 mg twice daily) resulted in a 10% increase in mean AUC of doxazosin, and no statistically significant changes in mean C_{max} and mean half-life of doxazosin. The 10% increase in the mean AUC for doxazosin with cimetidine is within intersubject variation (27%) of the mean AUC for doxazosin with placebo.

PREGNACY AND LACTATION:
Pregnancy:
For the hypertension indication:
As there are no adequate and well controlled studies in pregnant women, the safety of doxazosin during pregnancy has not been established. Accordingly, during pregnancy, doxazosin should be used only if the potential benefit outweighs the risk. Although no teratogenic effects were seen in animal testing, reduced foetal survival was observed in animals at extremely high doses Doxazosin is contraindicated during lactation as the drug accumulates in milk of lactating rats and there is no information about the excretion of the drug into the milk of lactating women.
Breastfeeding
Alternatively, mothers should stop breast-feeding when treatment with Doxazosin is necessary

ADVERSE REACTION:

Commonly reported side effects of doxazosin include: dizziness, fatigue, vertigo, hypertension, symptomatic orthostatic hypotension, malaise, and orthostatic effect. Other side effects include: syncope, drowsiness, and edema.

Some side effects of doxazosin may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Doxazosin has no or negligible influence on the ability to drive and use machines.

OVERDOSE:
Should over dosage lead to hypotension, the patient should be immediately placed in a supine, head down position. Other supportive measures should be performed if thought appropriate in individual cases. Since doxazosin is highly protein bound, dialysis is not indicated.

If this measure is inadequate, shock should first be treated with volume expanders. If necessary, vasopressor should then be used. Renal function should be monitored and supported as needed.

Since doxazosin is highly protein bound, dialysis is not indicated.

INCOMPATIBILITY:
Not applicable

SHELF LIFE:
36 months

PACKAGING:
10 tablets are packed in Alu / PVC blister and such 10 blisters are packed in a printed carton along with pack insert.

STORAGE CONDITION:
Store in a dry place below 30°C.

MANUFACTURED BY:
Cian Healthcare Pvt. Ltd.
Khasra No.: 248, Village Sisona, Bhagwanpur,
Roorkee, Haridwar, Uttarakhand, India.