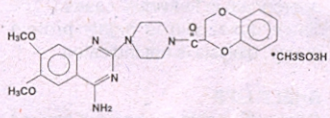
Pfizer

کارڈورا
Cardura®
(Doxazosin Mesylate)

DESCRIPTION
Cardura® (doxazosin mesylate) is a quinazoline compound that is a selective inhibitor of the alpha1 subtype of alpha-adrenergic receptors. The chemical name of doxazosin mesylate is 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(1,4-benzodioxan-2-ylcarbonyl) piperazine methanesulfonate. The empirical formula for doxazosin mesylate is $C_{23}H_{25}N_5O_5 \cdot CH_4O_3S$ and the molecular weight is 547.6. It has the following structure:



THERAPEUTIC INDICATIONS
- **Hypertension**
  Cardura® is indicated for the treatment of hypertension and can be used as the initial agent to control blood pressure in the majority of patients. In patients not adequately controlled on a single antihypertensive agent Cardura® may be used in combination with another agent such as a thiazide diuretic, a beta-blocker, a calcium antagonist or an angiotensin-converting enzyme inhibitor.

- **Benign Prostatic Hyperplasia**
  Cardura® is indicated for the treatment of clinical symptoms in benign prostatic hyperplasia (BPH) and for reduced urinary flow associated with BPH. Cardura® may be used in BPH patients who are either hypertensive or normotensive. While the blood pressure changes in normotensive patients with BPH are clinically insignificant, patients with hypertension and BPH have had both conditions effectively treated with doxazosin monotherapy.

POSOLOGY AND METHOD OF ADMINISTRATION
Cardura® may be administered either in the morning or in the evening.

Hypertension: The full dosage range of Cardura® is 1-16 mg daily. It is recommended that therapy be initiated at 1 mg given once daily for one or two weeks to minimize the potential for postural hypotension and/or syncope (see section **Special warnings and precautions for use**). The dosage may then be increased to 2 mg once daily for additional one or two weeks. If necessary the daily dosage should then be increased gradually at similar intervals to 4 mg, 8 mg, and 16 mg as determined by patient response to achieve the desired reduction in blood pressure. The usual dose is 2-4 mg once daily.

Benign Prostatic Hyperplasia: The recommended initial dosage of Cardura® is 1 mg given once daily to minimize the potential for postural hypotension and/or syncope (see section **Special warnings and precautions for use**). Depending on the individual patient's urodynamics and BPH symptomatology, dosage may then be increased to 2 mg and thereafter to 4 mg and up to the maximum recommended dose of 8 mg. The recommended titration interval is 1-2 weeks. The usual recommended dose is 2-4 mg once daily.

Use in Elderly: Normal adult dosage is recommended.

Use In Renally Impaired Patients: Since the pharmacokinetics of Cardura® are unchanged in patients with renal insufficiency, and there is no evidence that Cardura® aggravates existing renal dysfunction, the usual dosages may be used in these patients.

Use in Hepatically Impaired Patients: See section **Special warnings and precautions for use**.

Use in Children: The safety and efficacy of Cardura® in children have not been established.

CONTRAINDICATIONS
Cardura® (doxazosin) is contraindicated in patients with a known hypersensitivity to quinazolines, doxazosin, or any of the inert ingredients.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Postural Hypotension / Syncope: As with all alpha-blockers, a very small percentage of patients have experienced postural hypotension evidenced by dizziness and weakness, or rarely loss of consciousness (syncope), particularly with the commencement of therapy (see section **Posology and method of administration**). When instituting therapy with any effective alpha-blocker, 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 doxazosin therapy.

Use with PDE-5 Inhibitors: Concomitant administration of doxazosin with a PDE-5 inhibitor should be used with caution as it may lead to symptomatic hypotension in some patients.

Impaired Hepatic Function: As with any drug wholly metabolized by the liver, doxazosin should be administered with caution to patients with evidence of impaired hepatic function

Intraoperative Floppy Iris Syndrome: The Intraoperative Floppy Iris Syndrome (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with alpha$_1$ blockers. As IFIS may lead to increased procedural complications during the operation, current or past use of alpha blockers should be made known to the ophthalmologic surgeon in advance of surgery.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
Use with PDE-5 Inhibitors: (see section **Special warnings and precautions for use - Use with PDE-5 Inhibitors).**

Other: 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. Doxazosin has been administered without any adverse drug interaction in clinical experience with

thiazide diuretics, fusemide, beta-blockers, non-steroidal anti-inflammatory drugs, antibiotics, oral hypoglycemic drugs, uricosuric agents, or anticoagulants.

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.

PREGNANCY AND LACTATION

Although no teratogenic effects were seen in animal testing with doxazosin, reduced fetal survival was observed in animals at extremely high doses. These doses were approximately 300 times the maximum human recommended dose. Animal studies have shown that doxazosin accumulates in breast milk.

As there are no adequate and well controlled studies in pregnant or nursing women, the safety of doxazosin during pregnancy or lactation has not yet been established. Accordingly, during pregnancy or lactation, doxazosin should be used only when in the opinion of the physician, the potential benefit outweighs the potential risk.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The ability to engage in activities such as operating machinery or operating a motor vehicle may be impaired, especially when initiating doxazosin therapy.

UNDESIRABLE EFFECTS

Hypertension: In controlled clinical trials, the most common reactions associated with Cardura® were of a postural type (rarely associated with syncope) or non-specific and included:

- **Ear and Labyrinth Disorders:** vertigo
- **Gastrointestinal Disorders:** nausea
- **General Disorders and Administration Site Conditions:** asthenia, edema, fatigue, malaise
- **Nervous System Disorders:** dizziness, headache, postural dizziness, somnolence, syncope
- **Respiratory, Thoracic and Mediastinal Disorders:** rhinitis

Benign Prostatic Hyperplasia: Experience in controlled clinical trials in BPH indicates a similar adverse event profile to that seen in hypertension.

In post-marketing experience, the following additional adverse events have been reported:

- **Blood and Lymphatic Disorders:** leukopenia, thrombocytopenia
- **Ear and Labyrinth Disorders:** tinnitus
- **Eye Disorders:** blurred vision, IFIS (Intraoperative Floppy Iris Syndrome) (see section **Special warnings and precautions for use**).
- **Gastrointestinal Disorders:** abdominal pain, constipation, diarrhea, dyspepsia, flatulence, mouth dry, vomiting
- **General Disorders and Administrations Site Conditions:** pain
- **Hepatobiliary Disorders:** cholestasis, hepatitis, jaundice
- **Immune System Disorders:** allergic reaction
- **Investigations:** abnormal liver function tests, weight increase
- **Metabolism and Nutrition:** anorexia
- **Musculoskeletal and Connective Tissue Disorders:** arthralgia, back pain, muscle cramps, muscle weakness, myalgia
- **Nervous System Disorders:** hypoesthesia, paresthesia, tremor
- **Psychiatric Disorders:** agitation, anxiety, depression, insomnia, nervousness
- **Renal and Urinary Disorders:** dysuria, hematuria, micturition disorder, micturition frequency, nocturia, polyuria, urinary incontinence
- **Reproductive System and Breast Disorders:** gynecomastia, impotence, priapism, retrograde ejaculation
- **Respiratory, Thoracic and Mediastinal Disorders:** bronchospasm aggravated, coughing, dyspnea, epistaxis
- **Skin and Subcutaneous Tissue Disorders:** alopecia, pruritus, purpura, skin rash, urticaria
- **Vascular Disorders:** hot flushes, hypotension, hypotension postural

The following additional adverse events have been reported in marketing experience among patients treated for hypertension but these, in general, are not distinguishable from symptoms that might have occurred in the absence of exposure to Cardura®

OVERDOSAGE

Should overdosage 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.

SHELF LIFE

Cardura® should not be used beyond the expiry date i.e. 3 years

HOW SUPPLIED

Cardura® (doxazosin) is available with the following presentations

- 2 mg tablets : 2x10's blister pack
- 4 mg tablets : 2x10's blister pack

DOSAGE

Use as directed by the physician.

INSTRUCTIONS

Avoid exposure to heat & sunlight.
Store in a dry place at room temperature.
Keep out of the reach of children.

CAUTION

To be sold on the prescription of a registered medical practitioner only.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: دوا کو گرمی اور سورج کی روشنی سے بچائیں۔
کمرے کے درجہ حرارت پر خشک جگہ میں رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
تاکید: صرف رجسٹرڈ میڈیکل پریکٹشنر کے نسخہ پر فروخت کریں۔

Pfizer
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Pfizer Pakistan Ltd.
B-2, S.I.T.E., Karachi, Pakistan.
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