United Pharmaceuticals

CURCARD®

Doxazosin Mesilate

Description:

CURCARD® (Doxazosin Mesilate) is a quinazoline-derivative postsynaptic alpha 1-adrenergic blocking agent. The drug is chemically and pharmacologically related to Prazosin and Terazosin.

Doxazosin reduces peripheral vascular resistance and blood pressure as a result of its vasodilating effects; the drug produces both arterial and venous dilation. Doxazosin reduces blood pressure in both supine and standing patients; the effect is most pronounced on standing blood pressure, and postural hypotension can occur. Doxazosin generally causes no change in heart rate or cardiac output in the supine position. Cardiovascular responses to exercise (e.g., increased heart rate and cardiac output) are maintained during Doxazosin therapy.

Effects of Doxazosin on the cardiovascular system are mediated by the drug's activity at alphalreceptor sites on vascular smooth muscle. Alpha 1-Adrenergic receptors also are located in nonvascular smooth muscle (e.g., bladder trigone and sphincters, GI tract and sphincters, prostate adenoma and capsule, ureters, uterus) and in nonmuscular tissues (e.g., CNS, liver, kidneys). Because of the prevalence of ct-receptors on the prostate capsule, prostate adenoma, and the bladder trigone and the relative absence of these receptors on the bladder body, a-blockers decrease urinary outflow resistance in men. Doxazosin may improve to a limited extent the serum lipid profile (e.g., small increases in high-density lipoprotein cholesterol concentrations [HDL] and HDL/total cholesterol ratio, small decreases in low-density lipoprotein cholesterol [LDL], total cholesterol, and triglyceride concentrations), and can reduce blood glucose and serum insulin concentrations. The drug does not appear to affect plasma renin activity appreciably.

Properties:

Doxazosin is well absorbed after oral doses, peak plasma concentrations occurring 2 to 3 hours after a dose. Oral bioavailability is about 65%. It is extensively metabolized in the liver, and excreted in feces as metabolites and a small amount of unchanged drug. Elimination from plasma is biphasic, with a mean terminal half-life of about 22 hours. The pharmacokinetics is not altered in patients with renal impairment. Doxazosin is about 98% bound to plasma proteins and is not removed by dialysis. Studies in animals indicate that Doxazosin accumulates in breast milk.

Indications:

Hypertension: **CURCARD®** is indicated for the treatment of hypertension and can be used as the sole agent to control blood pressure in the majority of patients. In patients inadequately controlled on single antihypertensive therapy, **CURCARD®** may be used in combination with a thiazide diuretic, beta-adrenoceptor blocking agent, calcium antagonist or an angiotensin-converting enzyme inhibitor.

Benign prostatic hyperplasia: **CURCARD®** is indicated for the treatment of urinary outflow obstruction and symptoms associated with benign prostatic hyperplasia (BPH). Doxazosin 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 **CURCARD®** mono-therapy.

Dosage and administration:

CURCARD® tablets are swallowed with some liquid and may be administered in the morning or the evening.

Hypertension: **CURCARD®** is used in a once daily regimen: the initial dose is 1mg, to minimise the potential for postural hypotension and/or syncope. Dosage may then be increased to 2 mg after an additional one or two weeks of therapy and thereafter, if necessary to 4mg. The majority of patients who respond to **CURCARD®** 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 16 mg.

Benign prostatic hyperplasia: The recommended initial dosage of **CURCARD®** is 1mg given once daily to minimize the potential for postural hypotension and/or syncope. Depending on the individual patient's urodynamics and BPH symptomatology dosage may then be increased to 2mg 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 daily.

Children: Doxazosin is not licensed for use in children.

Elderly: Normal adult dosage.

Patients with renal impairment: Since there is no change in pharmacokinetics in patients with impaired renal function, the usual adult dose of **CURCARD®** is recommended.

Hepatic impairment: Use with caution; avoid in severe impairmentno information available.

Contraindications:

Doxazosin is contraindicated in:

- Patients with a known hypersensitivity to quinazolines (e.g. Prazosin, Terazosin, Doxazosin), or any of the excipients.
- Patients with a history of orthostatic hypotension.
- Patients with benign prostatic hyperplasia and concomitant congestion of the upper urinary tract, chronic urinary tract infection or bladder stones.
- During lactation.
- Patients with hypotension (for benign prostatic hyperplasia indication only).

Doxazosin is contraindicated as monotherapy in patients with either overflow bladder or anuria with or without progressive renal insufficiency.

Precautions:

Postural Hypotension/Syncope:

Initiation of Therapy: 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. Therefore, it is prudent medical practice to monitor blood pressure on initiation of therapy to minimize the potential for postural effects. 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 in patients with Acute Cardiac Conditions:

As with any other vasodilatory anti-hypertensive agent it is prudent medical practice to advise caution when administering Doxazosin to patients with the following acute cardiac conditions:

- Pulmonary oedema due to aortic or mitral stenosis.
- High-output cardiac failure.
- Right-sided heart failure due to pulmonary embolism or pericardial effusion.
- Left ventricular heart failure with low filling pressure.

Use in Hepatically Impaired patients: As with any drug wholly metabolized by the liver, Doxazosin should be administered with particular caution to patients with evidence of impaired hepatic function. Since there is no clinical experience in patients with severe hepatic impairment use in these patients is not recommended.

Use with PDE-5 Inhibitors: Concomitant administration of Doxazosin with phosphodiesterase-5-inhibitors (e.g. sildenafil, tadalafil, and vardenafil) should be done with caution as both drugs have vasodilating effects and may lead to symptomatic hypotension in some patients. To reduce the risk of orthostatic hypotension it is recommended to initiate the treatment with phosphodiesterase-5-inhibitors only if the patient is hemodynamically stabilized on alpha-blocker therapy. Furthermore, it is recommended to initiate phosphodiesterase-5-inhibitor treatment with the lowest possible dose and to respect a 6-hour time interval from intake of Doxazosin.

Use in patients undergoing cataract surgery: Risk of intra-operative floppy iris syndrome

Driving: May affect performance of skilled tasks e.g. driving

Use during pregnancy and lactation:

Pregnancy: No evidence of teratogenicity; use Doxazosin only when potential benefit outweighs risk.

Breast-feeding: Doxazosin accumulates in milk-avoid during breast feeding.

Drug interactions:

Doxazosin has the following interaction information:

Tadalafil: Enhanced hypotensive effect when Doxazosin given with Tadalafil.

Doxazosin belongs to alpha-blockers (post-synaptic) but Alpha-blockers (post-synaptic) has no interactions information.

Doxazosin belongs to alpha-blockers and will have the following interactions:

- ACE Inhibitors: Enhanced hypotensive effect when given with ACE inhibitors.
- Adrenergic Neurone Blockers: Enhanced hypotensive effect when alpha-blockers given with adrenergic neurone blockers.
- Alcohol: Enhanced hypotensive effect when alpha-blockers given with alcohol.
- Aldesleukin: Enhanced hypotensive effect when alpha-blockers given with aldesleukin.
- Alprostadil: Enhanced hypotensive effect when alpha-blockers given with alprostadil.
- General Anaesthetics: Enhanced hypotensive effect when alpha-blockers given with general anaesthetics.
- Angiotensin-II Receptor Antagonists: Enhanced hypotensive effect when alpha-blockers given with angiotensinII receptor antagonists.
- Antipsychotics: Enhanced hypotensive effect when alpha-blockers given with antipsychotics. Increased risk of toxicity with myelosuppressive drugs.
- Anxiolytics and Hypnotics: Enhanced hypotensive and sedative effects when alpha-blockers given with anxiolytics and hypnotics.
- Baclofen: Enhanced hypotensive effect when alpha-blockers given with baclofen.
- Beta-blockers: Enhanced hypotensive effect when alpha-blockers given with beta- blockers, also increased risk of first- dose hypotension with post-synaptic alpha-blockers such as prazosin. Since systemic absorption may follow topical application of beta-blockers to the eye the possibility of interactions, in particular, with drugs such as verapamil should be born in mind.
- Calcium-channel Blockers: Enhanced hypotensive effect when alpha-blockers given with calcium-channel blockers, also increased risk of first-dose hypotension with post- synaptic alpha-blockers such as Razosin. Dihydropyridine calcium channel blockers include Amlodipine, Felodipine, Isradipine, Lacidipine, Lercanidipine, Nicardipine, Nifedipine, and Nimodipine.
- Clonidine: Enhanced hypotensive effect when alpha-blockers given with Clonidine.
- Corticosteroids: Hypotensive effect of alpha-blockers antagonised by corticosteroids. Interactions do not generally apply to corticosteroids used for topical action (including inhalation) unless specified.
- Diazoxide: Enhanced hypotensive effect when alpha-blockers given with diazoxide.
- Diuretics: Enhanced hypotensive effect when alpha-blockers given with diuretics, also increased risk of first-dose hypotension with post-synaptic alpha- blockers such as prazosin.
- Hydralazine: Enhanced hypotensive effect when alpha-blockers given with Hydralazine.
- Levodopa: Enhanced hypotensive effect when alpha-blockers given with Levodopa.
- MAOIs: Enhanced hypotensive effect when alpha-blockers given with MAOIs.
- Methyldopa: Enhanced hypotensive effect when alpha-blockers given with methyldopa.
- Minoxidil: Enhanced hypotensive effect when alpha-blockers given with Minoxidil.
- Moxisylyte: Possible severe postural hypotension when alpha-blockers given with Moxisylyte.
- Moxonidine: Enhanced hypotensive effect when alpha-blockers given with Moxonidine.
- Nitrates: Enhanced hypotensive effect when alpha-blockers given with nitrates.
- NSAIDs: Hypotensive effect of alpha-blockers antagonized by NSAIDs. Interactions do not generally apply to topical NSAIDs.
- Oestrogens: Hypotensive effect of alpha-blockers antagonized by oestrogens. Interactions of combined oral contraceptives may also apply to combined contraceptive patches and vaginal rings.
- Sildenafil: Enhanced hypotensive effect when alpha-blockers given with Sildenafil (avoid alpha-blockers for 4 hours after Sildenafil).
- Sodium Nitroprusside: Enhanced hypotensive effect when alpha-blockers given with sodium Nitroprusside.
- Tizanidine: Enhanced hypotensive effect when alpha-blockers given with Tizanidine.
- Vardenafil: Enhanced hypotensive effect when alpha-blockers (excludes Tamsulosin) given with Vardenafil -separate doses by 6 hours.

Side effects:

Side-effects of alpha 1-selective alpha blockers include drowsiness, hypotension (notably postural hypotension), syncope, asthenia, dizziness, depression, headache, dry mouth, gastro-intestinal disturbances, oedema, blurred vision, intra-operative floppy iris syndrome (most strongly associated with tamsulosin), rhinitis, erectile disorders (including priapism), tachycardia, and palpitations. Hypersensitivity reactions including rash, pruritus and angioedema have also been reported ; also dyspnoea, coughing; fatigue, paraesthesia, sleep disturbance, anxiety, respiratory- tract infection, urinary-tract infection, influenza-like symptoms; back pain, myalgia; less commonly weight changes, flushing, tremor, agitation, micturition disturbance, epistaxis, arthralgia, tinnitus, gout, and alopecia; very rarely cholestasis, hepatitis, jaundice, bronchospasm, gynaecomastia, abnormal ejaculation, leucopenia, and thrombocytopenia.

Overdosage:

Should overdosage lead to hypotension, the patient should be immediately placed in a supine, head down position. Other supportive measures may be appropriate in individual cases.

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.

Storage conditions:

Store up to 30ºC.

Presentation:

CURCARD® 1: Each tablet contains Doxazosin Mesilate EP equivalent to 1 mg Doxazosin in packs of 20 tablets.

CURCARD® 4: Each tablet contains Doxazosin Mesilate EP equivalent to 4 mg Doxazosin in packs of 20 tablets.

Hospital packs are also available.

This is a medicament

· Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
· Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
· The doctor and the pharmacist are experts in medicine, its benefits and risks.
· Do not by yourself interrupt the period of treatment prescribed for you.
· Do not repeat the same prescription without consulting your doctor.
· Keep medicament out of the reach of children.

COUNCIL OF ARAB HEALTH MINISTERS
UNION OF ARAB PHARMACISTS

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