SCHEDULING STATUS: S3

PROPRIETARY NAMES (and Dosage Form):

Cardugen 1 mg (tablets)

Cardugen 2 mg (tablets)

Cardugen 4 mg (tablets)

COMPOSITION:

Doxazosin mesylate is a derivative, having the chemical name:
1-(4- amino- 6,7 – dimethoxy – 2 – quinazolinyl) - 4 - (1, 4 – benzodioxan – 2 - yl- carbonyl) piperazine methanesulphonate. It is a white powder, slightly soluble in methanol and sparingly soluble in water, ethanol, acetone and chloroform, and has a molecular weight of 547,6 (free base 451,5).

Each 1 mg, 2 mg and 4 mg Cardugen Tablet contains doxazosin mesylate equivalent to 1 mg, 2 mg and 4 mg free base respectively. Contains sugar.

PHARMACOLOGICAL CLASSIFICATION:

A.7.1 Vasodilators, hypotensive medicines.

PHARMACOLOGICAL ACTION:

Cardugen exerts a vasodilator effect via selective and competitive blockade of post-junctional alpha-1-adrenoceptors.

After oral administration, Cardugen is well absorbed with peak blood levels occurring at about 2 hours. The plasma elimination is biphasic with the terminal elimination half-life being 19 to 22 hours, hence providing the basis for once daily dosing. Cardugen is extensively metabolised with less than 5% excreted as the unchanged drug.
Maximum reduction in blood pressure normally occurs about 6 hours after dosing.
Most (98%) of plasma doxazosin is protein bound. In vitro data in human plasma indicates that Cardugen has no effect on protein binding of the drugs tested (digoxin, phenytoin, warfarin or indomethacin).

INDICATIONS:

Cardugen is indicated for the treatment of mild to moderate hypertension.

Cardugen is also indicated for the treatment of the urinary outflow obstruction and symptoms associated with benign prostatic hyperplasia (BPH). Cardugen may be used in BPH patients who are either hypertensive or normotensive.

CONTRAINDICATIONS:

Cardugen is contraindicated in patients with a known hypersensitivity to quinazolines.

Use in Children:

No experience is available on the use of Cardugen in children.

INTERACTIONS:

No adverse drug interaction has been noted in clinical experience to date with thiazide diuretics, furosemide, beta-blocking agents, antibiotics, oral hypoglycaemic drugs, uricosuric agents or anticoagulants.

Administration of doxazosin may reduce plasma concentrations of triglycerides, total and LDL-cholesterol and increase HDL-cholesterol. These potentially favourable effects on lipids persist when a thiazide-type diuretic is given concurrently. The long-term consequences of these drug-induced changes in lipids are not known.

PREGNANCY AND LACTATION:

The safety in pregnancy or lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Hypertension:

The initial dosage of Cardugen is 1 mg given once daily. Depending on the individual patient's response, dosage may then be increased after 1 – 2 weeks of therapy to 2 mg and thereafter at similar intervals to 4 mg, 8 mg and 16 mg to achieve the desired reduction in blood pressure. In patients not adequately controlled on a single antihypertensive agent, Cardugen may be used in combination with a thiazide diuretic or a beta-blocking agent.

Benign Prostatic Hyperplasia:

The initial dosage of Cardugen is 1 mg given once daily. 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. Blood pressure should be evaluated routinely in these patients.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

The most common reactions associated with Cardugen therapy are dizziness, headache, fatigue, vertigo, hypotension, oedema and asthenia. Other side-effects include abnormal vision, chest pain, depression, diarrhoea, dry mouth, dyspnoea, insomnia, nausea, nervousness, palpitation, rash, rhinitis, sexual dysfunction, somnolence, tachycardia and malaise.

Extremely rare cases of urinary incontinence were reported; this effect may be related to Cardugen's pharmacological action.

Cases of priapism and impotence have been reported in association with doxazosin.

The following have been reported in post-marketing experience: angina pectoris, myocardial infarction, cerebrovascular accidents, cardiac arrythmias and blurred vision.

Less frequent cases of non-specific gastric complaints such as abdominal pain, diarrhoea and vomiting and less frequent cases of agitation and tremor have also been reported. Cases of allergic drug reactions such as skin rashes, pruritis, purpura, jaundice and elevated liver transaminases and epistaxis have also been reported.

Driving/Use of Machinery:

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

Impaired Liver Function:

Special precautions must be taken in patients with impaired liver function.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See : Side effects and Special Precautions.

Since Cardugen is highly protein bound, dialysis is not indicated. Treatment is symptomatic and supportive.

IDENTIFICATON:

Cardugen 1 mg: White, round, biconvex tablets.

Cardugen 2 mg: White, round, biconvex tablets.

Cardugen 4 mg: White, round, biconvex tablets.

PRESENTATION:

1 mg: High density polyethylene bottles of 30, 100, or 1000 tablets, or Blister Packs of 30 tablets.

2 mg: High density polyethylene bottles of 30, 100, or 1000 tablets, or Blister Packs of 30 tablets.

4 mg: High density polyethylene bottles of 30, 100, or 1000 tablets, or Blister Packs of 30 tablets.

STORAGE INSTRUCTIONS:

Store below 25 °C. Protect from light. Keep original containers well closed. Do not remove blister from carton until required for use.

Keep out of reach of children.

REGISTRATION NUMBERS:

CARDUGEN 1 mg: 34/7.1/0271

CARDUGEN 2 mg: 34/7.1/0272

CARDUGEN 4 mg: 34/7.1/0273

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Mylan (Pty) Ltd.

Greenstone Hill Office Park,

Building 6, Emerald Boulevard

Modderfontein

Gauteng

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