ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORM(S), STRENGTH(S) OF THE MEDICINAL PRODUCT(S), ROUTE(S) OF ADMINISTRATION, APPLICANT(S)/ MARKETING AUTHORISATION HOLDER(S) IN THE MEMBER STATES

Note: This SPC, labelling and package leaflet is the version that was annexed to the Commission Decision on this Article 29 referral for doxazosin mesilate containing medicinal products. The text was valid at that time.

After the Commission Decision, the Member State competent authorities will update the product information as required. Therefore, this SPC, labelling and package leaflet may not necessarily represent the current text.

Member State	Marketing Authorisation Holder	Applicant	Invented name	Strength	Pharmaceutical Form	Route of administration
Czech Republic		Ratiopharm GmbH Graf-Arco-Strasse 3 89079 Ulm, Germany Tel: 0049 731 40202 Fax: 0049 731 4027330	Doxazosin-ratiopharm retard 4 mg	4 mg	Prolonged release tablets	Oral
Denmark	Pharmcom Oy Keijumaki 6B 30 02130 Espoo Finland Tel: 00358 407 075670 Fax: 00358 94524872		Cargoreg 4 mg depottabletter	4 mg	Prolonged release tablets	Oral
Hungary		Ratiopharm Hungaria Kft. Uzoki utca 36/a 1145 Budapest, Hungary Tel: 0036 1 2732730 Fax: 0036 1 2732731	Doxazosin-ratiopharm retard 4 mg tabletta	4 mg	Prolonged release tablets	Oral
Poland		Ratiopharm GmbH Graf-Arco-Strasse 3 89079 Ulm, Germany Tel: 0049 731 40202 Fax: 0049 731 4027330	Doxazosin-ratiopharm retard PR4	4 mg	Prolonged release tablets	Oral
Slovakia		Ratiopharm GmbH Graf-Arco-Strasse 3 89079 Ulm, Germany Tel: 0049 731 40202 Fax: 0049 731 4027330	Doxazosin-ratiopharm retard 4 mg	4 mg	Prolonged release tablets	Oral

Member State	Marketing Authorisation Holder	Applicant	Invented name	Strength	Pharmaceutical Form	Route of administration
United Kingdom		Ratiopharm GmbH Graf-Arco-Strasse 3 89079 Ulm, Germany Tel: 0049 731 40202 Fax: 0049 731 4027330	DoxaCard XL 4 mg prolonged release tablets	4 mg	Prolonged release tablets	Oral

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARY(IES) OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF Cardoreg 4 mg prolonged release tablets and associated names (see Annex I)

CHMP was of the opinion that the bioequivalence was sufficiently established after single dose administration in two different bioequivalence studies (study 463/04 and 1995/04-05) and after multiple dose administration (study 5208/02-3) according to the CHMP guidelines. The observed differences in T_{max} are modest and the C_{max} of the test tablet is not higher than the innovator tablet. It is unlikely that these differences will result in clinically relevant adverse events. The test product has shown consistent single dose performance across the studies and sufficient reassurance has been provided that the steady state results submitted are representative of other batches. The food-interaction study was not performed according to the CHMP guidelines. However, results of this study indicated that when administered with food no clinical significant differences exist between both products. Since 2002 more than 44,000,000 generic tablets of this formulation have been supplied to the market and that thousands of subjects have been switched from the originator product to the generic product. Up to now there were no adverse events potentially related to a faster release of doxazosin reported. The company made additionally a commitment for post-marketing surveillance.
In conclusion essential similarity has been sufficiently demonstrated. Any additional doubts regarding essential similarity are overcome by a commitment for post-marketing surveillance of the applicant. The CHMP is of the opinion the product does not differ significantly from the originator in terms of efficacy and safety.

GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Whereas

- The scope of the referral was to agree whether Cardoreg 4mg prolonged release tablets differ significantly with regards to the release profile from the originator product with potential for increased incidence of adverse events such as dizziness and hypotension, whether there were significant differences in performance of test batches in the single dose phase of studies 5208 and 1995 and whether the applicant has deviated from CHMP guidelines on the design of the bioequivalence studies, particularly in relation to the effect of food with concern regarding the adequate sensitivity of to detect a difference between products,
- It is unlikely that the potential differences observed between the reference product and the generic versions influence the information in the Summary of Product Characteristics (SPC),
- The SPC, labelling and package leaflet proposed by the applicant has been assessed based on the documentation submitted, the scientific discussion within the Committee and the new wording proposed in the updated Guideline on SPC dated October 2005 and the latest QRD template,

the CHMP has recommended the granting of the Marketing Authorisation(s) for which the Summary of Product Characteristics, labelling and package leaflet are set out in Annex III for Cardoreg 4 mg prolonged release tablets and associated names (see Annex I).

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cardoreg 4 mg prolonged release tablets and associated names

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One prolonged-release tablet contains 4 mg doxazosin (as mesilate).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release tablet

White round biconvex tablets marked “DL” on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Essential hypertension

Symptomatic treatment of benign prostatic hyperplasia.

4.2 Posology and method of administration

Cardoreg 4 mg prolonged release tablets and associated names can be taken with or without food. The tablets must be swallowed whole with a sufficient amount of liquid. The prolonged-release tablets should not be chewed, divided or crushed.

The maximum recommended dose is 8 mg doxazosin once daily.

Essential hypertension:
Adults: Usually 4 mg doxazosin once daily. If necessary, the dosage may be increased to 8 mg doxazosin once daily.

Cardoreg 4 mg prolonged release tablets and associated names can be used as sole agent or in combination with another medicinal product e.g. a thiazide diuretic, beta-adrenoceptor blocking agent, calcium antagonist or an ACE-inhibitor.

Symptomatic treatment of prostatic hyperplasia:
Adults: Usually 4 mg doxazosin once daily. If necessary, the dosage may be increased to 8 mg doxazosin once daily.

Cardoreg 4 mg prolonged release tablets and associated names may be used in benign prostatic hyperplasia (BPH) patients who are either hypertensive or normotensive, as the blood pressure changes in normotensive patients are clinically insignificant. In hypertensive patients both conditions are treated concomitantly.

Elderly: Same dosage as for adults.

Patients with renal impairment: Since there is no change in pharmacokinetics in patients with impaired renal function, and since there are no signs that doxazosin aggravates existing renal impairment, the usual dose can be used in these patients.

Patients with hepatic impairment: Cardoreg 4 mg prolonged release tablets and associated names should be given with particular caution to patients with evidence of impaired liver function. In patients

with severe hepatic impairment clinical experience is lacking and therefore the use of doxazosin prolonged release tablets is not recommended (see section 4.4).

Children and adolescents: Cardoreg 4 mg prolonged release tablets and associated names is not recommended for patients under the age of 18 years.

4.3 Contraindications

- Hypersensitivity to the active substance, other quinazolines (e.g. prazosin, terazosin), or to any of the excipients
- Benign hyperplasia and concomitant congestion of the upper urinary tract, chronic urinary tract infections or bladder stones
- Overflow bladder, anuria or progressive renal insufficiency
- History of oesophageal or gastrointestinal obstruction or decreased lumen diameter of the gastrointestinal tract
- Lactation.

4.4 Special warnings and precautions for use

Patients with acute heart diseases:
Cardoreg 4 mg prolonged release tablets and associated names should be administered with caution in patients with the following acute heart diseases: Pulmonary oedema as a result of aortic or mitral stenosis, heart failure at high output, right sided heart failure as a result of pulmonary embolism or pericardiac effusion and left sided ventricular heart insufficiency with low filling pressure.

In hypertensive patients with one or more additional risk factors for cardiovascular disease, doxazosin should not be used as a single agent for the first-line treatment of hypertension due to a possible increased risk for development of heart failure.

On initiation of therapy or increasing of dose the patient should be monitored to minimise the potential for postural effects, e.g. hypotension and syncope. In patients treated for benign prostatic hyperplasia and without hypertension mean blood pressure changes are small, but hypotension, dizziness, fatigue occur in 10 – 20% of the patients and oedema and dyspnoea occur in less than 5% of patients. Special care should be taken with hypotensive patients or patients with known orthostatic dysregulation taking doxazosin prolonged release tablets to treat benign prostatic hyperplasia (BPH). They should be informed about the potential risk for injuries and measures of precaution to minimise orthostatic symptoms.

Patients with hepatic impairment:
Cardoreg 4 mg prolonged release tablets and associated names should be administered with caution in patients with signs of mild to moderate hepatic impairment (see section 5.2). Since no clinical experience from patients with severe hepatic insufficiency exists, use in these patients is not recommended. Caution is also recommended when doxazosin is administered concomitantly with medicinal products which may influence hepatic metabolism (e.g. cimetidine).

Cardoreg 4 mg prolonged release tablets and associated names should be used with care in patients with Diabetic Autonomic Neuropathy.

Cardoreg 4 mg prolonged release tablets and associated names may influence plasma renin activity and urinary excretion of vanillylmandelic acid. This should be considered when interpreting laboratory data.

4.5 Interactions with other medicinal products and other forms of interaction

Doxazosin is highly bound to plasma proteins (98%). *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 together with thiazide diuretics, furosemide, beta-blocking agents, antibiotics, oral

hypoglycaemic agents, uricosuric agents, or anticoagulants without adverse drug interactions. Doxazosin potentiates the blood pressure lowering effect of other antihypertensives. Non-steroidal antirheumatics or estrogens may reduce the antihypertensive effect of doxazosin. Sympathomimetics may reduce the antihypertensive effect of doxazosin; doxazosin may reduce blood pressure and vascular reactions to dopamine, ephedrine, epinephrine, metaraminol, methoxamine and phenylephrine.

There are no studies concerning interactions with agents influencing hepatic metabolism.

4.6 Pregnancy and lactation

There are no adequate data from the use of doxazosin prolonged release tablets in pregnant women. Animal studies have shown reduced foetal survival at high doses (see section 5.3). Cardoreg 4 mg prolonged release tablets and associated names should not be used during pregnancy unless clearly needed.

Cardoreg 4 mg prolonged release tablets and associated names is contraindicated during lactation as the medicinal product accumulates in the milk of lactating rats (see section 5.3) and there is no information about the excretion of the medicinal product into human breast milk. Alternatively, breast-feeding must be stopped, if treatment with Cardoreg 4 mg prolonged release tablets and associated names is unavoidable.

4.7 Effects on ability to drive and use machines

Cardoreg 4 mg prolonged release tablets and associated names has moderate influence on the ability to drive and use machines, especially at the beginning of therapy.

4.8 Undesirable effects

The occurrence of adverse reactions are mainly due to the pharmacological properties of the medicinal product. The majority of the adverse reactions were transient.

The adverse reaction profile in clinical trials with patients with benign prostatic hyperplasia corresponded to the one seen in hypertension.

The adverse reactions considered at least possibly related to treatment are listed below by body system organ class and absolute frequency. Frequencies are defined as very common (≥1/10); common (>1/100 to <1/10); uncommon (>1/1000 to <1/100); rare (>1/10 000 to <1/1000); very rare (<1/10 000).

Blood and lymphatic system disorders:
Very rare: Reduction of erythrocytes, leucocytes and thrombocytes

Metabolism and nutrition disorders:
Uncommon: thirst, hypokalaemia, gout
Rare: hypoglycaemia
Very rare: increase in serum urea.

Psychiatric disorders:
Common: apathia
Uncommon: nightmares, amnesia, emotional instability
Rare: depression, agitation

Nervous system disorders:
Common: muscle cramps, fatigue, malaise, headache, somnolence
Uncommon: tremor, muscular stiffness
Rare: paraesthesia

Eye disorders:

Common: accomodation disturbances
Uncommon: lacrimation, photophobia
Rare: blurred vision

Ear and labyrinth disorders:
Uncommon: tinnitus

Cardiac disorders:
Common: palpitations, chest pain
Uncommon: arrhythmia, angina pectoris, bradycardia, tachycardia, myocardial infarction

Vascular disorders:
Common: giddiness, dizziness, oedema, orthostatic dysregulation
Uncommon: postural hypotension, peripheral ischaemia, syncope
Rare: cerebrovascular disturbances

Respiratory, thoracic and mediastinal disorders:
Common: dyspnoea, rhinitis
Uncommon: epistaxis, broncho spasms, cough, pharyngitis
Rare: oedema of larynx

Gastrointestinal disorders:
Common: constipation, dyspepsia
Uncommon: anorexia, increased appetite, taste disturbances
Rare: abdominal discomfort, diarrhoea, vomiting

Hepatobiliary disorders:
Rare: icterus, increased liver values

Skin and subcutaneous tissue disorders:
Uncommon: alopecia, oedema of the face/general oedema
Rare: rash, pruritus, purpura

Musculoskeletal, connective tissue and bone disorders:
Uncommon: muscular pain, swelling of joints/arthralgia, muscle weakness

Renal and urinary disorders:
Common: frequent desire to micturate, increased micturation, delayed ejaculation
Uncommon: incontinence, micturation disturbances, dysuria
Rare: impotence, priapism
Very rare: increase of serum creatinine.

General disorders and administration site conditions:
Common: asthenia
Uncommon: flushing, fever/shiver, paleness
Rare: low body temperature in elderly

Particular caution:
Postural hypotension and in rare cases syncope may occur at the beginning of therapy, especially at very high doses but also when treatment is recommenced after a break.

4.9 Overdose

ymptoms:
Headache, dizziness, unconsciousness, syncope, dyspnoea, hypotension, palpitation, tachycardia, arrhythmia. Nausea, vomiting. Possibly hypoglycaemia, hypokalaemia.

Treatment:
Symptomatic treatment. Close control of blood pressure. Since doxazosin is strongly bound to plasma proteins dialysis is not indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Hypertension:
Administration of Cardoreg 4 mg prolonged release tablets and associated names in hypertensive patients causes a clinically significant reduction in blood pressure as a result of a reduction in systemic vascular resistance. This effect is thought to result from selective blockade of the alpha-1-adrenoceptors located in the vasculature. With once daily dosing, clinically significant reductions in blood pressure are present throughout the day and at 24-hours post dose. The majority of patients are controlled on the initial dose of 4 mg Cardoreg 4 mg prolonged release tablets and associated names . In patients with hypertension, the decrease in blood pressure during treatment with Cardoreg 4 mg prolonged release tablets and associated names was similar in both the sitting and standing position.

Patients treated with immediate release doxazosin tablets against hypertension can be transferred to Cardoreg 4 mg prolonged release tablets and associated names and the dose titrated upwards as needed, while maintaining effect and tolerability.

Habituation has not been observed during long-term treatment with doxazosin. Increase in plasma renin activity and tachycardia have rarely been seen during long-term treatment.

Doxazosin has a beneficial effect on blood lipids with significant increase of HDL/total cholesterol ratio (app. 4-13% of base line values), and significant reduction in total glycerides and total cholesterol. The clinical relevance of these findings is still unknown.

Treatment with doxazosin has been shown to result in regression of left ventricular hypertrophy, inhibition of platelet aggregation as well as enhanced capacity of tissue plasminogen-activator. The clinical relevance of these findings is still uncertain. Additionally, doxazosin improves insulin sensitivity in patients with impaired sensitivity to insulin, but also concerning this finding the clinical relevance is still uncertain.

Doxazosin has shown to be free of metabolic adverse effects and is suitable for treatment of patients with coexistent asthma, diabetes, left ventricular dysfunction or gout.

Prostatic hyperplasia:
Administration of Cardoreg 4 mg prolonged release tablets and associated names to patients with prostatic hyperplasia results in a significant improvement in urodynamics and symptoms as a result of a selective blockade of alpha-adrenoceptors located in the prostatic muscular stroma, capsule and bladder neck.
Most of the patients with prostatic hyperplasia are controlled with the initial dose.

Doxazosin has shown to be an effective blocker of 1A subtype of alpha-adrenoceptors which make up more than 70% of the adrenergic subtypes in prostate.

Throughout the recommended dosage range, Cardoreg 4 mg prolonged release tablets and associated names has only a minor or no effect on blood pressure in normotensive benign prostatic hyperplasia (BPH) patients.

5.2 Pharmacokinetic properties

Absorption:
After oral administration of therapeutic doses, doxazosin in Cardoreg 4 mg prolonged release tablets and associated names is well absorbed with peak blood levels gradually reached at 6 to 8 hours after dosing. Peak plasma levels are approximately one third of those of the same dose of immediate release doxazosin tablets. Trough levels at 24 hours are, however, similar. The pharmacokinetic properties of doxazosin in Cardoreg 4 mg prolonged release tablets and associated names lead to a minor variation in plasma levels. Peak/trough ratio of Cardoreg 4 mg prolonged release tablets and associated names is less than half that of immediate release doxazosin tablets.
At steady-state, the relative bioavailability of doxazosin from Cardoreg 4 mg prolonged release tablets and associated names compared to immediate release form was 54% at the 4 mg dose and 59% at the 8 mg dose.

Distribution:
App. 98% of doxazosin is protein-bound in plasma.

Biotransformation:
Doxazosin is extensively metabolised with <5% excreted as unchanged product. Doxazosin is primarily metabolised by O-demethylation and hydroxylation.

Elimination:
The plasma elimination is biphasic with the terminal elimination half-life being 22 hours and hence this provides the basic for once daily dosing

Elderly:
Pharmacokinetic studies with doxazosin in the elderly have shown no significant alterations compared to younger patients.

Renal impairment:
Pharmacokinetic studies with doxazosin in patients with renal impairment also showed no significant alterations compared to patients with normal renal function.

Liver impairment:
There are only limited data in patients with liver impairment and on the effects of medicinal products known to influence hepatic metabolism (e.g. cimetidine). In a clinical study in 12 subjects with moderate hepatic impairment, single dose administration of doxazosin resulted in an increase of AUC of 43% and a decrease in oral clearance of app. 40%. Doxazosin therapy in patients with hepatic impairment should be performed with caution (see section 4.4.).

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenicity. Studies in pregnant rabbits and rats at daily doses resulting in plasma concentrations 4 and 10 times the human exposure (C_{max} and AUC), respectively, revealed no evidence of harm to the foetus. A dosage regime of 82 mg/kg/day (8 times the human exposure) was associated with reduced foetal survival.

Studies in lactating rats given a single oral dose of radioactive doxazosin gave an accumulation in the breast milk with a maximum concentration of about 20 times greater than the maternal plasma concentration. Radioactivity was found to cross the placenta following oral administration of labelled doxazosin to pregnant rats.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Macrogol
Cellulose, microcrystalline
Povidone K 29-32
Butylhydroxytoluene (E321)
α-Tocopherol
Silica, colloidal anhydrous
Sodium stearyl fumarate

Tablet coat:
Methacrylic acid - ethyl acrylate copolymer (1:1) Dispersion 30 per cent
Silica, colloidal anhydrous
Macrogol 1300-1600
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVDC/aluminium blister.

Pack sizes: 20, 28, 30, 50, 98, 100 and 500 prolonged-release tablets (Normal blister: 20, 30, 50, 100, 500; calendar blister: 28, 98; unit dose blister: 30x1, 50x1, and 100x1)

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8 MARKETING AUTHORISATION NUMBER

[To be completed nationally]

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10 DATE OF REVISION OF THE TEXT

[To be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Cardoreg 4 mg prolonged release tablets and associated names {See Annex I]
Doxazosin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each prolonged-release tablet contains 4 mg of doxazosin (as mesilate).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

20 prolonged-release tablets
28 prolonged-release tablets
30 prolonged-release tablets
50 prolonged-release tablets
98 prolonged-release tablets
100 prolonged-release tablets
500 prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Cardoreg 4 mg prolonged release tablets and associated names [See Annex I]
Doxazosin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Cardoreg 4 mg prolonged release tablets and associated names [See Annex I]
(Doxazosin)

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do NOT pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1 WHAT CARDOREG 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES IS AND WHAT IT IS USED FOR

Your doctor may have prescribed Cardoreg 4 mg prolonged release tablets and associated names because your blood pressure is high, which if left uncontrolled can increase the risk of heart disease or stroke. The active ingredient in your tablets, doxazosin, belongs to a group of medicines known as alpha-blockers. These medicines work by widening your blood vessels, making it easier for your heart to pump blood through them. This helps to lower raised blood pressure.

Or you may have been prescribed Cardoreg 4 mg prolonged release tablets and associated names because you have enlargement of the prostate gland (prostatic hyperplasia). This makes it difficult to pass urine. The prostate gland is just underneath the bladder in men. Cardoreg 4 mg prolonged release tablets and associated names works by relaxing muscle around the bladder exit and prostate gland, making it easier to pass urine.

2 BEFORE YOU TAKE CARDOREG 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES

Do not take Cardoreg 4 mg prolonged release tablets and associated names
- if you are allergic to doxazosin or to any of the ingredients listed above
- if you know that you are sensitive to quinazolines (e.g. prazosin, terazosin) which is the chemical family of medicines to which doxazosin belongs
- if you suffer or have suffered from any form of obstruction of the digestive tract
- if you have an infection or an obstruction of the urinary tract or bladder stones
- if you suffer from kidney problems, overflow incontinence (you do not feel the urge to urinate) or anuria (your body is not producing any urine)
- if you are breast-feeding

Take special care with Cardoreg 4 mg prolonged release tablets and associated names
- if you suffer from liver problems
- if you suffer from acute heart disease such as pulmonary oedema or heart failure

Taking other medicines
You should always tell your doctor about any medicines you are taking. This includes any medicines you have bought for yourself, as well as those prescribed for you by a doctor. Some medicines may interact with Cardoreg 4 mg prolonged release tablets and associated names . These include:

- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Other medicines used in the treatment of high blood pressure
- Oestrogens
- Dopamine, ephedrine, adrenaline, metaraminol, metoxamine, phenylephrine (medicines used for the treatment of heart problems)

Taking Cardoreg 4 mg prolonged release tablets and associated names with food and drink
Cardoreg 4 mg prolonged release tablets and associated names can be taken with or after food.

Pregnancy and breast-feeding
Do not take Cardoreg 4 mg prolonged release tablets and associated names if you are pregnant or breast-feeding. Speak to your doctor first.

Driving and using machines
Cardoreg 4 mg prolonged release tablets and associated names can cause drowsiness. Be especially careful when you take you first start taking the tablets. If this happens do not drive or operate machinery.

3 HOW TO TAKE CARDOREG 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES

Always take Cardoreg 4 mg prolonged release tablets and associated names exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The label on the carton will tell you how many tablets you should take and when. The tablets should be swallowed whole with a glass of water. Do not crush or chew the tablets.

Adults and the elderly:
The dose of Cardoreg 4 mg prolonged release tablets and associated names is the same whether you are taking it for high blood pressure or to treat the symptoms of prostatic hyperplasia. The usual dose is one tablet each day. Your doctor may increase your dose to the maximum recommended dose of two tablets each day.

If you take more Cardoreg 4 mg prolonged release tablets and associated names than you should
If you take too many tablets, the most likely symptoms would be a feeling of light-headedness or dizziness due to a fall in blood pressure. You should lie down on your back with your feet higher than your head. Contact your nearest casualty department or tell your doctor or pharmacist immediately. Take this leaflet and any left-over tablets with you, so the doctor knows what you have taken.

If you forget to take Cardoreg 4 mg prolonged release tablets and associated names
Try to take your tablets daily as prescribed. However, if you miss a dose, just take it as soon as you remember. Do not take two doses at the same time.

If you stop taking Cardoreg 4 mg prolonged release tablets and associated names
Do not stop taking your medicine without consulting your doctor.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4 POSSIBLE SIDE EFFECTS

Like all medicines, Cardoreg 4 mg prolonged release tablets and associated names can cause side effects, although not everybody gets them.

Common side effects that may occur (in between 1 in 10 people and 1 in 100 people) are:

- muscle cramps, tiredness, sleepiness, generally feeling unwell, headache
- palpitations, chest pain
- giddiness or dizziness especially on getting up from a sitting or lying position
- rhinitis (runny nose or stuffiness), shortness of breath
- constipation, indigestion or heartburn
- oedema (swelling of the feet or ankles),
- increased need to pass urine, increased volume of urine passed, delayed ejaculation
- weakness

Uncommon side effects that may occur (in between 1 in 100 people and 1 in 1000 people) are:

- thirst, low levels of potassium in the blood, gout
- nightmares, memory loss, mood changes
- muscle tremor, muscle stiffness
- watery eyes, intolerance to light
- ringing or noise in the ears
- irregular heartbeat, angina, slow or fast heartbeat,
- fainting, especially on getting up from a sitting or lying position,
- nosebleeds, difficulty in breathing, cough, inflammation of the throat
- lack of appetite or increased appetite, taste disturbances
- hair loss, swelling of the face or other parts of the body
- painful joints or muscles, muscle weakness
- incontinence, pain on passing urine
- flushing, fever, shivering

Rare side effects that may occur (in between 1 in 1000 people and 1 in 10,000 people) are:

- low blood sugar levels
- depression, agitation
- tingling in the hands and feet
- blurred vision
- swelling of the larynx (voice box)
- abdominal pain, diarrhoea, being sick
- jaundice, increases in liver enzymes
- rash, itching, redness
- inability to achieve an erection, painful persistent erections.

Very rare side effects that may occur (in less than 1 in 10,000 people) are:

- low white blood cells: low blood platelets, which may result in bruising or easy bleeding

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5 HOW TO STORE CARDOREG 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES

Keep out of the reach and sight of children.

Do not use Cardoreg 4 mg prolonged release tablets and associated names after the expiry date which is stated on the carton and blister.

This medicinal product does not require any special storage conditions.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6 FURTHER INFORMATION

What Cardoreg 4 mg prolonged release tablets and associated names contains:

- The active substance is doxazosin (as the mesilate).
  One prolonged-release tablet contains 4,85 mg doxazosin mesilate corresponding to 4 mg doxazosin
- The other ingredients are polyethylene oxide, microcrystalline cellulose, povidone, α-tocopherol, colloidal anhydrous silica, sodium stearyl fumarate, methacrylic acid – ethyl acrylate co-polymer (1:1), macrogol, and titanium dioxide (E171).

What Cardoreg 4 mg prolonged release tablets and associated names looks like and contents of the pack:

Cardoreg 4 mg prolonged release tablets and associated names are white, round, biconvex tablets with bossing “DL” on one side.
They are available in PVC/PVDC/aluminium blisters packs of 28 tablets [20, 30, 50, 98, 100 and 500 tablets].

Marketing Authorisation Holder and Manufacturer:

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:

[To be completed on finalisation of the procedure]

This leaflet was last approved in [To be completed nationally].