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
Estonia		STADA Arzneimittel AG Stadastr. 2-18, 61118 Bad Vilbel Germany Tel: 0049 6101 603301 Fax: 0049 6101 603151	Doxalfa 4 mg toimeainet prolongeeritult vabastavad tabletid	4 mg	Prolonged-release tablet	Oral
Latvia		STADA Arzneimittel AG Stadastr. 2-18, 61118 Bad Vilbel Germany Tel: 0049 6101 603301 Fax: 0049 6101 603151	Doxalfa 4 mg ilgstošās darbības tabletes	4 mg	Prolonged-release tablet	Oral
Lithuania		STADA Arzneimittel AG Stadastr. 2-18, 61118 Bad Vilbel Germany Tel: 0049 6101 603301 Fax: 0049 6101 603151	Doxalfa 4 mg pailginto atpalaidavimo tabletės	4 mg	Prolonged-release tablet	Oral
Netherlands		Cerntrafarm Services B.V. Nieuwe Donk 9, 4879 AC Etten-Leur The Netherlands Tel: 0031 765 081000 Fax: 0031 765 035614	Doxazosine retard CF 4mg, tabletten met gereguleerde afgifte	4 mg	Prolonged-release tablet	Oral
Spain		Laboratorio STADA, S.L. Frederic Mompou, 5 08960 Sant Just Desvern	DOXAZOSINA NEO STADA 4 mg comprimidos de	4 mg	Prolonged-release tablet	Oral

		Barcelona, Spain Tel: 0034 93 4738889 Fax: 0034 93 4737495	liberación prolongada EEG			
Sweden	STADA Arzneimittel AG Stadastr. 2-18, 61118 Bad Vilbel Germany Tel: 0049 6101 603301 Fax: 0049 6101 603151		Doxastad 4mg depottablett	4 mg	Prolonged-release tablet	Oral
United Kingdom		Genus Pharmaceuticals Benham Valence, Speen, Newbury, Berkshire RG20 8LU Tel: 01635 568400 Fax: 01635 568401	Doxadura XL 4 mg	4 mg	Prolonged-release tablet	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 Doxastad 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 (study5208/02-3) 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(IES) OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Whereas

- The scope of the referral was to agree whether Doxastad 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 Doxastad 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

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

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, with bossing “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

The tablets should be swallowed whole with a sufficient amount of liquid. The patient should not chew, divide or crush the tablet.

Doxastad 4 mg prolonged release tablets and associated names can be taken with or without food.

The maximum recommended dose is 8 mg doxazosin once daily.

Essential hypertension:
Adults:
Most patients treated with Doxastad 4 mg prolonged release tablets and associated names once daily achieve control of blood pressure. It may take up to four weeks to reach optimal effect. If necessary, the dose can thereafter be increased to 8 mg once daily depending on the clinical response.

Doxastad 4 mg prolonged release tablets and associated names can be used as monotherapy or in combination with another medicinal product e.g. a thiazide diuretic, a beta-adrenoceptor blocking agent, a calcium antagonist or an ACE-inhibitor if either of them alone does not provide sufficient effect.

Symptomatic treatment of Benign prostatic hyperplasia:
Adults:
Recommended dose is 4 mg once daily. Depending on clinical response, the dosage may be increased to 8 mg doxazosin once daily.

Doxazosin may be used in benign prostatic hyperplasia patients who are either hypertensive or normotensive, as the blood pressure reduction in normotensive patients is generally slight. Patients should be closely monitored in the initial phase of the treatment due to the risk of postural adverse events.

Elderly:
Same dosage recommendations 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, normal dose can generally be used in these patients.

Patients with hepatic impairment:
Doxazosin should be administered with caution in patients with signs of minor to moderate hepatic impairment. Since no clinical experience from patients with severe hepatic insufficiency exists, use in these patients is not recommended (see section 4.4).

Paediatric patients:
There are not sufficient data to recommend the use in children and adolescents.

4.3 Contraindications

- Hypersensitivity to the active substance, other quinazolines (e.g. prazosin, terazosin) or to any of the excipients.
- History of oesophageal or gastrointestinal obstruction or judged to be at increased risk for such obstruction.
- Benign prostatic hyperplasia and concomitant urinary outflow obstruction, chronic urinary tract infections or bladder stones
- Overflow bladder, anuria or progressive renal insufficiency

4.4 Special warnings and precautions for use

Abnormally short transport time through the gastrointestinal tract could lead to incomplete absorption.

As for other antihypertensives, including alpha-blocking agents, the patient should be monitored on initiation of therapy to minimise the potential risk for postural effects.

Simultaneous administration of sildenafil or other PDE-5 inhibitors to patients taking alpha-blocker therapy may lead to symptomatic hypotension in some patients (see section 4.5).

Patients with acute heart diseases:
As for other vasodilating antihypertensives, caution is recommended according to medical praxis, in patients with the following acute heart diseases:
- pulmonary oedema as a result of aortic or mitral stenosis
- heart failure at high output
- left or right sided heart failure as a result of pulmonary embolism, pericardial effusion, high output or low filling pressure

Patients with hepatic impairment:
Doxazosin, as other medicinal products metabolised by the liver, should be administered with caution in patients with signs of minor 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.

Use during lactation
Animal studies have shown that doxazosin accumulates in breast milk. The clinical safety during lactation has not been established, consequently use in nursing mothers is not recommended.

4.5 Interactions with other medicinal products and other forms of interaction

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 available concerning interactions with agents influencing hepatic metabolism.

Doxazosin may influence the plasma renin activity and urinary excretion of vanillylmandelic acid. This should be considered when analysing laboratory data.

Simultaneous administration of sildenafil or other PDE-5 inhibitors to patients taking alpha-blocker therapy may lead to symptomatic hypotension in some patients. Therefore, sildenafil doses above 25 mg should not be taken within 4 hours of taking an alpha-blocker (see section 4.4).

4.6 Pregnancy and lactation

There are no adequate data from the use of doxazosin in pregnant women. Although no teratogenic effects were noted in animal studies, Doxastad 4 mg prolonged release tablets and associated names should not be used during pregnancy unless clearly needed.

Animal studies have shown that doxazosin is accumulated in the milk. There is no information available on accumulation of doxazosin in human breast milk. Doxastad 4 mg prolonged release tablets and associated names should therefore not be administered to breastfeeding women. Interruption of breast-feed should be considered in cases of required continuation of doxazosin.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The following undesirable effects have been reported in controlled clinical trials with doxaszosin prolonged-release tablets.

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).

Vascular disorders
Common Dizziness, postural dizziness.

Respiratory, thoracic and mediastinal disorders
Common Rhinitis.

Gastrointestinal disorders
Common Diarrhoea, nausea, vomiting, gastritis.

General disorders

Common	Headache, fatigue, malaise, oedema, somnolence, asthenia, mouth dryness.

Rare cases of syncope in association with orthostatic hypotension have been observed.

The following adverse events have been reported in clinical use of immediate release tablets of doxazosin:

Blood and lymphatic system disorders: Thrombocytopenia, leukopenia.
Metabolism and nutrition disorders: Gout.
Psychiatric disorders: Nervousness.
Nervous system disorders: Tremor.
Eye disorders: Blurred vision.
Ear and labyrinth disorders*:* Tinnitus, vertigo.
Cardiac disorderst: Arrhythmia, tachycardia, palpitations, angina pectoris, myocardial infarction.
Vascular disorders: Cerebrovascular accidents.
Respiratory, thoracic and mediastinal disorders: Dyspnoea, cough, bronchial spasms, epistaxis.
Gastrointestinal disorders: Anorexia, obstipation, increased appetite.
Hepatobiliary disorders: Icterus, increased liver transaminases.
Skin and subcutaneous tissue disorders: Rash, pruritus, purpura.
Musculoskeletal and connective tissue disorders*:* Myalgia, arthralgia, muscle cramps.
Renal and urinary disorders: Increased diuresis, haematuria, urinary incontinence.
Reproductive system and breast disorders: Priapism and impotence.
General disorders and administration site conditions: Chest pain, agitation, facial flushing.

4.9 Overdose

Toxicity
There is limited data on the effect of overdoses. Syncope occurred in a fasting adult who had taken doxazosin 16 mg. A 13-year-old experienced moderate intoxication following a maximum dose of doxazosin 40 mg.

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

Treatment:
Ventricle emptying and charcoal if required. In cases of hypotension: lower the head position, provide intravenous fluids and if needed vasopressors (for instance noradrenaline or ephedrine). Provide symptomatic treatment as needed.

Since doxazosin is strongly bound to proteins dialysis is not indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Alpha-adrenoreceptor antagonists

ATC code: C02CA04
The generic name for the active substance in Doxastad 4 mg prolonged release tablets and associated names is doxazosin, which is a quinazoline derivative. Doxazosin has a vasodilating effect through selective and competitive blocking of postsynaptic alpha-1-receptors.

With once daily dosing, clinically significant reductions in blood pressure are present throughout the day and at 24-hours post dose.

Habituation has not been observed during long-term treatment with doxazosin immediate release tablets. 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). The clinical relevance of these findings is still unknown.

Doxazosin improves insulin sensitivity in patients with impaired sensitivity to insulin. Treatment with doxazosin immediate release tablets has been shown to result in regression of left ventricular hypertrophy. Studies on morbidity and mortality have not yet been terminated.

Hypertension:
Analysis of two dose-effect studies (including a total of 630 patients treated with doxazosin) have shown that patients treated with immediate release tablets in dosages of 1 mg, 2 mg or 4 mg are equally controlled on doxazosin prolonged-release tablets containing 4 mg.

Interim analysis of the study "Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial" (ALLHAT) shows that patients with hypertension and at least one other clinical risk factor for coronary heart disease treated with doxazosin are exposed to a doubled risk for chronic heart failure compared to patients treated with chlortalidone. Furthermore, they had 25% higher risk of developing clinically significant cardiovascular disorders. The doxazosin arm of ALLHAT was discontinued as a result of these findings. There was no difference in mortality.

The results are difficult to interpret due to various reasons such as differences in effect on systolic blood pressure and discontinuation of diuretics in the doxazosin-treated group prior to commencement of the treatment.

Benign Prostatic hyperplasia:
Doxazosin has been shown to inhibit phenylephrine induced contraction in the prostate. High levels of alpha-1-adrenoreceptors have been observed in the prostatic muscular stroma, the proximal part of the urethra and base of the urinary bladder, which medicates smooth muscle tonus in the prostatic part of the urethra. Blocking alpha-1-adrenoreceptors through doxazosin reduces the tonus of the smooth muscle in the prostatic part of the urethra which facilitates the urinary flow. This is the pharmacological basis for clinical use of doxazosin in treatment for benign prostatic hyperplasia.

Effect and safety studies (with a total of 1,317 patients treated with doxazosin) have only been performed in patients with a baseline of ≥ 12 on the International Prostate Symptom Score and a maximum urinary flow of <15 ml/sec. Data from these studies indicate that patients well controlled on immediate release tablets of doxazosin in doses of 1 mg, 2 mg or 4 mg are equally controlled on doxazosin 4 mg prolonged-release tablets.

5.2 Pharmacokinetic properties

Absorption:
After oral administration of therapeutic doses, doxazosin prolonged-release tablets are well absorbed with peak blood levels gradually reached at 6 to 8 hours after dosing. Peak plasma levels are approximately one third of the level obtained after administration of immediate release doxazosin tablets. Trough levels at 24 hours are, however, similar for both formulations.

The pharmacokinetic properties of doxazosin in prolonged-release tablets lead to a minor variation in plasma levels.

Peak/trough ratio of doxazosin prolonged-release tablets is less than half that of immediate release doxazosin tablets.

At steady-state, the relative bioavailability of doxazosin from prolonged-release tablets compared to that of immediate release form was 54% at the 4 mg dose and 59% at the 8 mg dose.
Concomitant intake of food results in a somewhat higher degree of absorption, AUC is 14% higher and C_{max} 23% higher compared with intake when fasting. C_{min} is unaffected by concomitant food intake.

Distribution:
Approximately 98% of doxazosin is protein-bound in plasma. Volume of distribution: 1 litre/kg.

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

Elimination:
Clearance of doxazosin is 1.3 ml/min/kg.
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 prolonged-release tablets in the elderly have shown no significant alterations compared to younger patients.

Renal impairment:
Pharmacokinetic studies with doxazosin immediate release tablets in patients with renal impairment did not show any significant alterations compared to that of patients with normal renal function.

Liver impairment:
There are only limited data concerning patients with liver impairment and on the effects of medicinal products known to influence hepatic metabolism (e.g. cimetidine). In a clinical study of 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 approximately 30%.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated toxicity, toxicity to reproduction, genotoxicity and carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Polyethylene oxide
Microcrystalline cellulose
Povidone
All-rac-α-Tocopherol
Colloidal anhydrous silica
Sodium stearyl fumarate
Butylhydroxytoluene (E321)

Tablet coat:
Methacrylic acid - ethyl acrylate copolymer (1:1)
Colloidal anhydrous silica
Macrogol
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

Blister (PVC/PVDC/aluminium)

Cartons with 10, 20, 28, 30, 50, 56, 60, 90, 98, 100, 140 (10x14) prolonged-release tablets
Calendar packs of 28 and 98 prolonged-release tablets
Unit dose pack of 50 x 1 prolonged-release tablets

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

BOX

1. NAME OF THE MEDICINAL PRODUCT

Doxastad 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

Contains butylhydroxytoluene (E321)

4. PHARMACEUTICAL FORM AND CONTENTS

10 Prolonged-release tablets
20 Prolonged-release tablets
28 Prolonged-release tablets
30 Prolonged-release tablets
50 Prolonged-release tablets
56 Prolonged-release tablets
60 Prolonged-release tablets
90 Prolonged-release tablets
98 Prolonged-release tablets
100 Prolonged-release tablets
140 Prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Take as directed by your doctor.
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

Doxastad 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

Doxastad 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 DOXASTAD 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES IS AND WHAT IT IS USED FOR

Your doctor may have prescribed Doxastad 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-1 antagonists. 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, and reduce the risk of heart disease.

Or you may have been prescribed Doxastad 4 mg prolonged release tablets and associated names to treat the symptoms of Benign Prostatic Hyperplasia (BPH). This condition causes enlargement of the prostate gland, which is just underneath the bladder in men. This makes it difficult to pass urine. Doxastad 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 DOXASTAD 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES

Do not take Doxastad 4 mg prolonged release tablets and associated names
- if you have ever suffered an allergic reaction (e.g. itching, reddening of the skin or difficulty breathing) to the active ingredient, doxazosin, or any of the other 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 have or have had any form of obstruction of the digestive tract
- if you have benign prostatic hyperplasia and concomitant congestion of the upper urinary tract, chronic urinary infectiond or bladder stones
- if you have overflow bladder, anuria or progressive renal insufficiency

Take special care with Doxastad 4 mg prolonged release tablets and associated names
- if you suffer from liver disease
- if you have suffered acute heart disease such as heart failure
- if you are undergoing dialysis
- if you are under 18 years of age

Before surgery and anaesthesia (even at the dentist), you should tell the doctor or dentist that you are taking Doxastad 4 mg prolonged release tablets and associated names .

If you are not sure what to do, ask your doctor or pharmacist.

Taking Doxastad 4 mg prolonged release tablets and associated names with other medicines
Tell your doctor if you are already taking any of the following:
- 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)
- Drugs indicated for the treatment of erectile dysfunction (PDE-5 inhibitor, e.g. sildenafil, tadalafil, vardenafil)

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

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

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

Driving and using machines
Doxastad 4 mg prolonged release tablets and associated names can cause drowsiness. Be especially careful when you take your first dose, if your dose is increased, or if you are starting to take your medicine again after not having taking it for some time. If you feel dizzy or light-headed, do not drive or operate machinery.

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

You must keep taking your Doxastad 4 mg prolonged release tablets and associated names as instructed by your doctor. The directions should be given on the label. Your pharmacist may also be able to help if you are not sure.

The dose of Doxastad 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 BPH. The usual dose is one tablet (4 mg) each day. Your doctor may increase your dose to the maximum recommended dose of two tablets each day.

Doxastad 4 mg prolonged release tablets and associated names have been specially designed to release the active ingredient slowly throughout the day. The tablets can be taken at any time of the day before, during or after meals. Choose a time that is convenient for you and take your tablets at this time each day. The tablets must be swallowed whole with a sufficient amount of water. Do not chew, divide or crush the tablets.

If you take more Doxastad 4 mg prolonged release tablets and associated names than you should
If you take too many tablets, the most likely symptoms of overdose 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. You should tell your doctor immediately and see your doctor as soon as possible.

If you forget to take use Doxastad 4 mg prolonged release tablets and associated names
If you miss a dose, do not worry. Simply take the next day's tablet when it is due. Do not take a double dose to make up for a forgotten tablet.

If you stop taking Doxastad 4 mg prolonged release tablets and associated names
Keep taking your tablets until your doctor tells you to stop.

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

4 POSSIBLE SIDE EFFECTS

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

Common side effects include (occurs in more than 1 patient of 100): dizziness, postural dizziness (dizziness as a result of getting up from a sitting or lying position), rhinitis (nasal stuffiness and/or runny nose), diarrhoea, nausea, vomiting, gastritis (inflammation of the lining of the stomach), headache, fatigue, oedema (swelling), somnolence, asthenia (weakness), mouth dryness.

Uncommon side effects include (occurs in less than 1 patient of 100): thrombocytopenia (low platelets, which may result in easy bleeding), leukopenia (low white blood cells), gout, nervousness, tremor (trembling), blurred vision, tinnitus (ringing or noise in the ears), vertigo (a feeling of dizziness or 'spinning'), arrythmia (a feeling of irregular heart beat), tachycardia (increased heart rate), palpitations, angina pectoris, myocardial infarction (heart attack), cerebrovascular accident (stroke), dyspnoea (shortage of breath), cough, bronchial spasms, epistaxis (nosebleed), anorexia (loss of appetite), obstipation (constipation), increased appetite, icterus (jaundice), liver enzyme increases, rash, pruritus (itching), purpura (rash caused by bleeding under the skin), myalgia (painful muscles), arthralgia (painful joints), muscle cramps, increased diuresis (increased volume of urine passed), haematuria (blood in the urine), urinary incontinence, priapism (painful persistent erection), impotence, chest pain, agitation , facial flushing.

Rare cases of syncope (faint) in association with orthostatic hypotension (low blood presssure as a result of getting up from a sitting or lying position) have been observed.

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.

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

Keep out of the reach and sight of children.

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

This medicinal product does not require any special storage conditions.

After you have been told to stop taking your tablets, return any unused tablets to your pharmacist for safe disposal. Only keep the tablets if your doctor tells you to. These measures will help to protect the environment.

6 FURTHER INFORMATION

What Doxastad 4 mg prolonged release tablets and associated names contains

- The active substance is doxazosin (as mesilate).
- The other ingredients are polyethylene oxide, microcrystalline cellulose, povidone, butylhydroxytoluene (E321), all-rac-α-Tocopherol, colloidal anhydrous silica, sodium stearyl fumarate, methacrylic acid ethyl acrylate copolymer (1:1) dispersion 30%, macrogol, and titanium dioxide (E171).

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

The tablets are white, round, biconvex tablets with “DL” embossed on one side.
Your medicine is available in PVC/PVDC/aluminium blister packs containing 28 tablets [10, 20, 30, 50, 56, 60, 90, 98, 100, 140 (10x14) 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].