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	Name	Strength	Pharmaceutical Form	Route of administration
Denmark	Arrow Generics UK Ltd Unit 2 Eastman Way Stevenage Hertfordshire, SG1 4SZ United Kingdom Tel 00 44 207 612 7612 Fax 00 44 207 612 7620		Doxazosin "Arrow", 4mg depottabletter	4 mg	Prolonged release tablets	Oral
Portugal		Arrowblue Produtos Farndacêuticos S.A., Torre Fernão Magalhães, 10˚ Esq., Av. D. João II - Lisboa, Portugal Tel 00 351 21 896 51 05 Fax 00 351 21896 51 06	Doxazosin Arrow 4mg comprimido de libertação prolongada	4 mg	Prolonged release tablets	Oral
Slovenia		Arrow Generics UK Ltd Unit 2 Eastman Way Stevenage Hertfordshire, SG1 4SZ United Kingdom Tel 00 44 207 612 7612 Fax 00 44 207 612 7620	Doksazosin Arrow 4mg tablete s podaljšanim sproščanjem	4 mg	Prolonged release tablets	Oral
United Kingdom		Arrow Generics UK Ltd Unit 2 Eastman Way Stevenage Hertfordshire, SG1 4SZ United Kingdom Tel 00 44 207 612 7612 Fax 00 44 207 612 7620	Cardozin XL 4mg	4 mg	Prolonged release tablets	Oral

ANNEX II

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

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF Doxazosin "Arrow" 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 Doxazosin "Arrow" 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 Doxazosin "Arrow" 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

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 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"

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Essential hypertension
- Symptomatic treatment of benign prostatic hyperplasia.

4.2 Posology and method of administration

The tablets can be taken with or without food. The tablets must be swallowed whole with a sufficient amount of liquid. The 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.

Doxazosin 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.

Doxazosin 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 (see section 4.4).

Patients with hepatic impairment: Doxazosin 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 is not recommended. (see section 4.4).

Children and adolescents: Doxazosin is not recommended for use in children and adolescents due to a lack of clinical experience.

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 esophageal or gastrointestinal obstruction or decreased lumen diameter of the gastrointestinal tract
- Lactation.

4.4 Special warnings and precautions for use

Doxazosin is not considered appropriate as first-line treatment, this does not exclude the second- or third-line use in combination with other types of antihypertensives.

Patients with acute heart diseases:
Doxazosin 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 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:
Doxazosin 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).

Doxazosin should be used with care in patients with Diabetic Autonomic Neuropathy.

Doxazosin 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.

4.6 There are no studies concerning interactions with agents influencing hepatic metabolism.Pregnancy and lactation

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

Doxazosin 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 doxazosin is unavoidable.

4.7 Effects on ability to drive and use machines

Doxazosin has a minor or moderate influence on the ability to drive and use machines, especially at the beginning of therapy. Some patients may experience impaired ability to react.

4.8 Undesirable effects

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

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

The following adverse reactions have been report:

Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1, 000, <1/100); rare (>1/10, 000, <1/1, 000); very rare (<1/10, 000), including isolated reports

Blood and the 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, bronchospasms, cough, pharyngitis
Rare : oedema of larynx

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

Hepato-biliary 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

Symptoms:
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 doxazosin 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 doxazosin. In patients with hypertension, the decrease in blood pressure during treatment with doxazosin was similar in both the sitting and standing position.

Patients treated with immediate release doxazosin tablets against hypertension can be transferred to doxazosin prolonged-release 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 doxazosin 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, doxazosin 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 Doxazosin Retard Arrow 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 lead to a minor variation in plasma levels. Peak/trough ratio of doxazosin prolonged-release is less than half that of immediate release doxazosin tablets.

At steady-state, the relative bioavailability of doxazosin from doxazosin prolonged-release 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: 28, 30, 56, 98, and 100 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

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Doxazosin Retard Arrow 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

28 prolonged-release tablets
30 prolonged-release tablets
56 prolonged-release tablets
98 prolonged-release tablets
100 prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For 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: {MM/YYYY}

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

BN: {number}

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

Doxazosin Retard Arrow 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: {MM/YYYY}

4. BATCH NUMBER

BN: {number}

5. OTHER

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Doxazosin Retard Arrow 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 Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names is and what it is used for
2. Before you take Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names
3. How to take Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names
4. Possible side effects
5. How to store Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names
6. Further information

1 WHAT DOXAZOSIN RETARD ARROW 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES IS AND WHAT IT IS USED FOR

Doxazosin is one of a group of medicines called alpha-blockers. They are used to treat high blood pressure or the symptoms caused by enlargement of the prostate gland in men.

In patients taking Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names to treat high blood pressure (hypertension), doxazosin works by relaxing the blood vessels so that blood passes through them more easily. This helps to lower blood pressure.

In patients with enlargement of the prostate gland, Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names is taken to treat poor and/or frequent passing of urine. This is common in patients with enlargement of the prostate gland. Doxazosin works by relaxing muscle around the bladder exit and prostate gland so urine is passed more easily.

2 BEFORE YOU TAKE DOXAZOSIN RETARD ARROW 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES

Do not take Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names
- if you are allergic (hypersensitive) to doxazosin or any of the other ingredients of Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names
- 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 any kind of congestion or blockage in your urinary tract, an infection of the urinary tract or have bladder stones
- if you have a serious kidney disorder (anuria or progressive renal insufficiency)
- if you suffer from a loss of bladder control (bladder overflow)
- if you have or have ever had any form of obstruction of the digestive tract
  if you are breast-feeding.

- If you have any kind of congestion or blockage in your urinary tract, an infection of the urinary tract or have 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 have or have had in the past any form of obstruction of the digestive tract.

Take special care with Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names
- if you have problems with your heart or a history of heart disease
- if you have liver disease or you are taking medicines to control the way your liver works such as cimetidine or if you are undergoing dialysis
- if you suffer from diabetic autonomic neuropathy, a disease associated with diabetes which affects your nervous system.
- If you are under 18 years of age.

If you are planning to have surgery and anaesthesia (even at the dentist) you should tell your doctor or dentist that you are taking Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names .

Taking other medicines
Tell your doctor if you are already taking any of the following as they may interact with your medicine:

- medicines to lower your blood pressure including fosinopril and lisinopril as Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names can increase their effect
- certain non-steroidal medicines used to treat rheumatism or the female hormone, estrogen, as these can reduce the effect of Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names
- medicines which work on the nervous system such as dopamine, ephedrine, epinephrine, metaraminol, methoxamine and phenylephrine as these can also reduce the effect of Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names.

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

Taking Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names with food and drink
Doxazosin Retard Arrow 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.

Pregnancy and breast-feeding
Pregnancy
Do not take Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names if you are pregnant unless your doctor tells you to. If you become pregnant whilst taking this medicine you should contact your doctor as soon as possible.

Breast-feeding
You must not breast-feed whilst you are taking Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names can affect your judgement and concentration. When you start taking your tablets, make sure that your senses are not affected before you drive or operate machinery.

3 HOW TO TAKE DOXAZOSIN RETARD ARROW 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES

Always take Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names exactly as your doctor told you. You should check with your doctor or pharmacist if you are not sure.

Your tablets should be swallowed whole with a sufficient amount of liquid. Do not chew, crush or divide them. The tablets can be taken at any time of the day and before, during or after meals. Choose a time that is convenient for you and take your tablet at this time each day.

The usual dose of Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names is one tablet (4 mg) taken as a single dose each day.

Your doctor may wish to increase your dose to 8 mg per day. This is the maximum daily dose of Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names.

Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names is not recommended for children and adolescents under the age of 18 years.

If you take more Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names than you should:
You may get a headache, feel dizzy, sick or faint, and your heart may beat faster than normal. You should contact your doctor immediately or go to the nearest casualty department. Remember to take the pack and any remaining tablets with you.

If you forget to take Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names:
Do not take the missed dose or a double dose to make up for the one you missed. Take your next dose at the normal time.

If you stop taking Doxazosin Retard Arrow 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, Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names can cause side effects, although not everybody gets them.

The following side effects have been reported:

Common (affecting less than one person in 10 but more than one person in 100):
Muscle pain, tiredness, a general feeling of being unwell or weakness, headache, sleepiness, problems with focussing your eyes, palpitations, chest pain, giddiness, dizziness, swelling, faintness or dizziness when standing up from a sitting or lying position, shortness of breath, runny nose (rhinitis), constipation, indigestion, an increased desire or need to urinate and delayed ejaculation.

Uncommon (affecting less than one person in 100 but more than one person in 1,000): low levels of potassium in the blood, gout, increased thirst, nightmares, forgetfulness (amnesia), emotional instability, tremor, muscle stiffness, increased tear production, abnormal intolerance to light, ringing in the ears (tinnitus), heart flutters, angina, an increase or slowing of the heart rate, heart attack, low blood pressure especially on getting up from a sitting or lying position, vascular problems, nose bleeds, tightening of the chest, cough, throat inflammation, eating disorders (anorexia), increased appetite, taste disturbances, hair loss, swelling of the face and joints, joint pain, muscle weakness, incontinence, difficulty with or pain on urinating, flushing, fever (shivers) and loss of colour.

Rare (affecting less than one person in 1,000 but more than one person in 10,000): depression, high blood sugar levels, agitation, pins and needles, blurred vision, stroke, swelling of the voice box, stomach pain, diarrhoea, vomiting (being sick), jaundice, increased liver enzymes in the blood, rash, itching or reddening of

the skin, impotence, painful, persistent erection of the penis and low body temperature (especially in the elderly).

Very rare (affecting less than one person in 10,000): a reduction in red and white cells in the blood and an increase in urea and creatinine levels in the blood.

You may feel faint or dizzy when standing up from a sitting or lying position especially at the beginning of your treatment or if you restart your treatment after a break. If this happens do not worry but make sure that you do not drive, operate machinery or carry out any activity which might be dangerous should you feel faint. If these symptoms persist or become a problem please contact your doctor.

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

5 HOW TO STORE DOXAZOSIN RETARD ARROW 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES:

Keep out of the reach and sight of children.

Do not use Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names after the expiry date which is stated on the carton after EXP:. The expiry date refers to the last day of that month.

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 Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names contains:

The active substance is doxazosin (as doxazosin mesilate).

The other ingredients in the tablet core are macrogol, microcrystalline cellulose, povidone, butylhydroxytoluene (E-321), α-tocopherol, silica colloidal anhydrous and sodium stearyl fumarate. The other ingredients in the tablet coat are methacrylic copolymer, silica colloidal anhydrous, macrogol and titanium dioxide (E-171)).

What Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names looks like and contents of the pack:
Your medicine is in the form of prolonged-release tablets. The tablets are white, round and biconvex with the embossing ‘DL’.

Doxazosin Retard Arrow 4 mg prolonged release tablets and associated names are available in blister packs of 28, 30, 56, 98 and 100 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:
Marketing Authorisation Holder:
Arrow Generics Limited, Unit 2, Eastman Way, Stevenage, Hertfordshire, SG1 4SZ, United Kingdom

Manufacturer:

Arrow Generics Limited, Unit 4/5 Willsborough Cluster, Clonshaugh Industrial Estate, Clonshaugh, Dublin 17, Republic of Ireland.

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

[To be completed nationally]

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