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
Denmark	Generics [UK] Ltd., Station Close, Potters Bar, Herts,EN6 1TL. UK Tel: 00 44 1707 853000 Fax: 00 44 1707 650734		Doxagamma	4mg	Prolonged-release tablet	oral
United Kingdom		Generics [UK] Ltd., Station Close, Potters Bar, Herts,EN6 1TL. UK Tel: 00 44 1707 853000 Fax: 00 44 1707 650734	Doxzogen XL 4mg Tablets	4mg	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 Doxagamma 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 Doxagamma 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 Doxagamma 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

Doxagamma 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”

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Essential hypertension
- Symptomatic treatment of benign prostatic hyperplasia.

4.2 Posology and method of administration

Doxagamma 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.

Doxagamma 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.

Doxagamma 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: 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: Doxagamma 4 mg prolonged release tablets and associated names are 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 ract 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

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 form injuries and measures of precaution to minimize 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.
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 in pregnant women. Animal studies have shown reduced foetal survival at high doses (see section 5.3). Doxagamma 4 mg prolonged release tablets and associated names should not be used during pregnancy unless clearly needed.

Doxagamma 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 Doxagamma 4 mg prolonged release tablets and associated names is unavoidable.

4.7 Effects on ability to drive and use machines

Doxagamma 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

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, 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 Doxagamma 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 Doxagamma 4 mg prolonged release tablets and associated names. In patients with hypertension, the decrease in blood pressure during treatment with Doxagamma 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 Doxagamma 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 Doxagamma 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, Doxagamma 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 Doxagamma 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 Doxagamma 4 mg prolonged release tablets and associated names lead to a minor variation in plasma levels. Peak/trough ratio of Doxagamma 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 Doxagamma 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 82mg/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 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 labeled 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 blisters
Pack sizes: 10, 20, 28, 30, 50, 56, 60, 90, 98, 100, 140 (10 x 14) tablets
Calendar packs of 28 and 98

Unit dose 50 x 1

HDPE tablet container

Pack sizes: 100, 250 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

Doxagamma 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 mesylate).

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
The tablets should be swallowed whole. Must not be chewed, divided or crushed.
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

Lot

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

Doxagamma 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

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

HDPE TABLET CONTAINER

1. NAME OF THE MEDICINAL PRODUCT

Doxagamma 4 mg prolonged release tablets and associated names
doxazosin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

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

3. LIST OF EXCIPIENTS

Contains butylhydroxytoluene (E321)

4. PHARMACEUTICAL FORM AND CONTENTS

100 prolonged-release tablets
250 prolonged-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
The tablets should be swallowed whole. Must not be chewed, divided or crushed.
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

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Doxagamma 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 DOXAGAMMA 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES IS AND WHAT IT IS USED FOR

Your medicine is in the form of a 'prolonged-release' tablet. It contains Doxazosin, which belongs to a group of medicines called alpha-blockers. Doxagamma 4 mg prolonged release tablets and associated names can treat high blood pressure (hypertension) by relaxing the blood vessels in the body and lowering blood pressure. Doxagamma 4 mg prolonged release tablets and associated names can also be given to men suffering from an enlarged prostate gland, as it can relax the muscles allowing urine to be passed more easily.

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

Do not take Doxagamma 4 mg prolonged release tablets and associated names
- if you have taken medicine containing Doxazosin or a similar medicine eg. Prazosin, and you suffered an allergic reaction
- if you are allergic to any of the tablet ingredients
- if you have or have had a blockage in your gut
- if you have kidney problems such as bladder stones, difficulty passing urine or suffer from frequent urine infections.

Take special care with Doxagamma 4 mg prolonged release tablets and associated names

- if you have heart disease or a heart condition
- if you have liver problems
- if you have diabetes

- if you need a blood test as Doxagamma 4 mg prolonged release tablets and associated names can affect some test results.

Tell your doctor if any of the above apply to you.

Taking other medicines
Tell your doctor if you are already taking any of the following:
- other medicine to lower blood pressure
- painkillers called non-steroidal anti-inflammatory medicine (NSAIDs) eg. Ibuprofen
- medicine containing Estrogen
- medicine containing Dopamine, Metaraminol, Methoxamine, Adrenaline (Epinephrine)

cough and cold remedies as they may contain Ephedrine, Phenylephrine.

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

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

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

Driving and using machines
Do not drive or operate machinery if you feel less alert while taking this medicine. This is more likely at the start of treatment or if the doctor increases your dose.

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

Your doctor has decided which dose is best for you. Follow your doctor's instructions and do not change the dose yourself. You should check with your doctor or pharmacist if you are not sure.

- Swallow the tablets whole with a full glass of water
- Take with or without food
- Do not chew, break or crush the tablets.

Adults including the elderly
The usual starting dose is one Doxagamma 4 mg prolonged release tablets and associated names tablet once a day. If necessary, your doctor may increase this dose to the maximum of two tablets once a day.

To treat hypertension, your doctor may give you another medicine to take along with Doxagamma 4 mg prolonged release tablets and associated names .
Doxagamma 4 mg prolonged release tablets and associated names is unlikely to affect your blood pressure unless you suffer from hypertension.

Your 'modified release' tablets have been specially designed to slowly release the medicine from the tablet shell. The shell does not break down but passes through your body. The empty tablet will be passed out in your stools. Do not worry if sometimes you notice the tablet shell in your stools.

If you take more Doxagamma 4 mg prolonged release tablets and associated names than you should

Contact your doctor or nearest hospital casualty department immediately. Take any remaining tablets and the container with you.

If you forget to take Doxagamma 4 mg prolonged release tablets and associated names
Take it as soon as you remember. If it is almost time for your next dose though, do not double the dose just carry on as before.

If you stop taking Doxagamma 4 mg prolonged release tablets and associated names
Do not suddenly stop taking your medicine as this may cause serious changes in your blood pressure.

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

4 POSSIBLE SIDE EFFECTS

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

Common side effects, seen in more than 1 in 100 patients but less than 1in 10, include dizziness, giddiness, feeling unusually tired or generally unwell, swelling of the ankles, palpitations, headache, chest pain, sleepiness, muscle cramp, constipation, indigestion, breathlessness, runny nose, delayed ejaculation, frequent urge to pass urine and blurred vision.
Uncommon effects, seen in more than 1 out of 1,000 patients but less than 1 in 100 patients, include swelling of the face and body, feeling faint, cold fingers and toes,, dizziness on standing, a racing or irregular heart beat, a slow heart beat, angina, severe chest pain, difficulty breathing, tremor, muscle stiffness, weakness or pain, pain or swelling of joints, change in appetite, hair loss, nose bleeds, cough, sore swollen throat, low blood potassium levels, feeling thirsty, gout, nightmares, loss of memory, mood changes, loss of bladder control or less frequent urge to pass urine, ringing in the ears and changes in taste.
Rare side effects, seen in more than 1 in 10,000 patients but less than 1 out of 1,000, include depression, feeling restless, pins and needles, an allergic rash, itchy red skin, stomach pain, diarrhoea, being sick, a hoarse voice, fainting, loss of consciousness, jaundice, liver changes, low blood sugar, impotence, persistent erection.
Very rare effects seen in less than 1 in 10,000 patients include blood changes and an increase in blood and creatinine levels.

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 DOXAGAMMA 4 MG PROLONGED RELEASE TABLETS AND ASSOCIATED NAMES

Keep out of the reach and sight of children.

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

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 Doxagamma 4 mg prolonged release tablets and associated names contains

- The active substance is 4 mg of doxazosin as doxazosin mesilate.
- The other ingredients are macrogol, microcrystalline cellulose, povidone, butylhydroxytoluene (E321), alpha-tocopherol, anhydrous colloidal silica, sodium stearyl fumarate, methacrylic acid copolymer and titanium dioxide (E171)

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

Doxagamma 4 mg prolonged release tablets and associated names tablets are white, round, biconvex tablets with bossing “DL”.
They are available in PVC/PVDC/aluminium blisters packs of 28 tablets [10, 20, 30, 50, 56, 60, 90, 98, 100, 140 (10 x 14) tablets and in HDPE tablet containers of 100, 250 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:

[See Annex I - To be completed nationally]

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