

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

PA 282/80/3

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Vasodur 4 mg Tablets.

#### 3 PHARMACEUTICAL FORM

Tablet

Plain capsule shaped, white with 'D4' on one side and a breakline on reverse.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic Indications

*Hypertension:*

Vasodur tablets are indicated for the treatment of hypertension and can be used to control blood pressure in most hypertensive patients. In patients inadequately controlled on single antihypertensive therapy, Vasodur may be used in conjunction with a thiazide diuretic beta-adrenoceptor blocking agent, calcium antagonist or an angiotensin-converting enzyme inhibitor.

##### 4.2 Posology and method of administration

*Adults:*

*Hypertension:*

Vasodur tablets are initially used once a day: the initial dose is 1mg. Dosage may then be increased after one or two weeks of therapy to 2mg and thereafter, if necessary to 4mg. The majority of patients who respond to doxazosin will do so at a dose of 4mg or less. Dosage can be further increased if required to 8mg or the maximum recommended dose of 16mg.

*Children:*

There is insufficient experience of the drug to recommend the use of Vasodur tablets in children.

*Elderly:*

Normal adult dosage.

*Patients with renal impairment:*

Since there is no significant variation in pharmacokinetics in patients with impaired renal function the usual adult dose of Vasodur tablets is recommended. Vasodur tablets are not dialysable.

*Impaired liver function:*

As with any drug completely metabolised by the liver, Vasodur tablets should be administered with caution to patients with evidence of impaired hepatic function (refer to section 4.4 special warnings and precautions for use).

##### 4.3 Contraindications

Vasodur tablets are contraindicated in patients with a known hypersensitivity to quinazolines.

*Use during lactation:*

Results from animal studies have shown that doxazosin accumulates in breast milk. The clinical safety of Vasodur tablets during lactation has not been established; as a result doxazosin is contraindicated in nursing mothers.

#### 4.4 Special warnings and precautions for use

*Impaired liver function:*

As with any drug completely metabolised by the liver, Vasodur tablets should be administered with caution to patients with evidence of impaired hepatic function (see 4.2 Posology and Method of Administration).

An excessive hypotensive effect may occur in some patients following soon after initial treatment often in persons who have shown evidence of over reaction with other antihypertensives and usually with the initial dose. It is recommended that the initial dose should be given when the patient is not required to undertake any activity such as driving or operating machinery.

The mean terminal half-life of doxazosin is 22 hours. This may be prolonged in patients with congestive heart failure. The rate of dose adjustment may need to be slowed.

In some patients with left ventricular failure, the decrease in left ventricular filling associated with vigorous therapy may result in a significant fall in cardiac output and systemic blood pressure after administration of doxazosin. These effects should be kept in mind when introducing therapy and continuous adjustment of dose used.

#### 4.5 Interaction with other medicinal products and other forms of interaction

Doxazosin is highly bound to plasma proteins (98%). *In vitro* data in human plasma demonstrates that doxazosin has no effect on protein binding of the drugs tested (digoxin, phenytoin, warfarin or indometacin). No adverse drug interactions have been identified with thiazide diuretics, furosemide, beta-blocking agents, non-steroidal anti-inflammatory drugs, antibiotics, oral hypoglycaemic drugs, uricosuric agents, or anticoagulants.

#### 4.6 Pregnancy and lactation

*Use during pregnancy:*

Although no teratogenic effects were seen in animal testing, reduced foetal survival was observed in animals at extremely high doses. The doses were in the region of 300 times the maximum recommended human dose. As there are no adequate and well controlled studies in pregnant women, the safety of Vasodur tablets use during pregnancy is yet to be established. Hence, doxazosin should be used only when, in the opinion of the physician, potential benefit outweighs potential risk.

*Use during lactation:*

Contraindicated. See 4.3 above.

#### 4.7 Effects on ability to drive and use machines

The ability to drive or use machinery may be impaired, especially when initiating therapy.

#### 4.8 Undesirable effects

*Hypertension:*

In clinical trials the most common reactions associated with Vasodur tablets therapy were of a postural type, (rarely associated with fainting) or non-specific and included: dizziness, headache, fatigue/malaise, postural dizziness, vertigo, oedema, asthenia, somnolence, nausea and rhinitis.

*The post marketing experience of doxazosin shows the following additional adverse events to have been reported:*

Rare cases of non-specific gastric complaints such as abdominal pain, diarrhoea and vomiting; rare cases of agitation

and tremor.

Rare cases of urinary incontinence were reported; this could be related to the pharmacological action of doxazosin.

Isolated reports of priapism and impotence have been reported to be associated with alpha-1-antagonists, including doxazosin.

Rare cases of skin rash, pruritus, thrombocytopenia, purpura, epistaxis, leucopenia, haematuria, cholestasis, hepatitis, jaundice, abnormal liver function tests, and blurred vision have also been reported.

The following additional adverse events have been reported in post marketing experience among patients treated for hypertension. In general, these are not distinguishable from symptoms that might have occurred in the absence of exposure to doxazosin: tachycardia, palpitations, chest pain, angina pectoris, myocardial infarction, cerebrovascular accidents and cardiac arrhythmias.

## 4.9 Overdose

Should overdosage lead to hypotension, the patient should be placed in a supine, head down position as soon as possible. Other supportive measures may be appropriate in individual cases. Since doxazosin is highly protein bound, dialysis is not indicated.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Doxazosin is a potent and selective post-junctional alpha 1-adrenoceptor antagonist. This action results in a decrease in systemic blood pressure. Doxazosin is appropriate for oral administration in a once daily basis in patients with essential hypertension.

Doxazosin has been shown to be free of adverse metabolic effects and is suitable for use in patients with coexistent diabetes mellitus, gout and insulin resistance.

Doxazosin is suitable for use in patients with co-existent asthma, left ventricular hypertrophy and in elderly patients. Treatment with doxazosin has been shown to result in regression of left ventricular hypertrophy, inhibition of platelet aggregation and enhanced activity of tissue plasminogen activator. Additionally, doxazosin improves insulin sensitivity in patients with diabetic impairment.

In addition to doxazosin tablets antihypertensive effect, long term studies have shown a modest reduction in plasma total cholesterol, LDL cholesterol and triglyceride concentrations and therefore may be of particular benefit to hypertensive patients with concomitant hyperlipidaemia.

### 5.2 Pharmacokinetic properties

Following oral administration in humans (young male adults or the elderly of either sex), doxazosin is well absorbed and approximately two thirds of the dose is bioavailable. The mean plasma elimination half life is 22 hours therefore making the drug acceptable for once daily administration.

Doxazosin is extensively metabolised in man and in the animal species tested, with the faeces being the main route of excretion.

After oral administration of doxazosin the plasma concentrations of the metabolites are low. The most active (6'hydroxy) metabolite is present in man at one fortieth of the plasma concentration of the parent compound which suggests that the antihypertensive activity is in the main due to doxazosin.

### 5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Lactose monohydrate  
Magnesium stearate  
Microcrystalline cellulose  
Sodium lauryl sulphate  
Sodium starch glycolate, type A

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf Life

2 years.

### 6.4 Special precautions for storage

None

### 6.5 Nature and contents of container

Vasodur 4 mg Tablets are available in clear PVC (254µ)/ Aluminium foil (25µ) blister strips in calendar or random foil packs of 28 tablets.

### 6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special instructions.

## 7 MARKETING AUTHORISATION HOLDER

Norton Healthcare Ltd T/A  
Ivax Pharmaceuticals UK  
Albert Basin,  
Royal Docks,  
London, E16 2QJ  
UK

## 8 MARKETING AUTHORISATION NUMBER

PA 282/80/3

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 7<sup>th</sup> March 2003.

Date of last renewal: 7<sup>th</sup> March 2003.

**10 DATE OF REVISION OF THE TEXT**

December 2004.