

VASCOTEN – PACKAGE INSERT

1. NAME OF THE MEDICINAL PRODUCT

Vascoten 50mg Tablet
Vascoten 100mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Vascoten 50mg tablet contains 50mg of atenolol
Each Vascoten 100mg tablet contains 100mg of atenolol
For the full list of excipients, see section 6.1.

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3. PHARMACEUTICAL FORM

Film-coated tablet.

Vascoten 50mg: red, round, concave film-coated tablets, embossed “S” on one side and deep scored on the other side with diameter of nucleus 9.0mm.

Vascoten 100mg: white, round, concave film-coated tablets, embossed “H” on one side and deep scored on the other side with diameter of nucleus 11.0mm.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Hypertension.
- Angina pectoris.
- Cardiac arrhythmias.
- Myocardial infarction. Early and late intervention.

4.2. Posology and method of administration

Posology

The dose must always be adjusted to individual requirements of the patients, with the lowest possible starting dosage. The following are guidelines.

Adults

Hypertension

One tablet daily. Most patients respond to 100 mg daily given orally as a single dose. Some patients, however, will respond to 50 mg given as a single daily dose. The effect will be fully established after one to two weeks. A further reduction in blood pressure may be achieved by combining atenolol with other antihypertensive agents. For example, co-administration of atenolol with a diuretic, provides a highly effective and convenient antihypertensive therapy.

Angina

Most patients with angina pectoris will respond to 100 mg given orally once or 50 mg given twice daily. It is unlikely that additional benefit will be gained by increasing the dose.

Cardiac Arrhythmias

A suitable initial dose of atenolol is 2.5mg (5ml) injected intravenously over a 2.5 minute period (i.e. 1mg/minute). This may be repeated at 5 minute intervals until a response is observed, up to a maximum dosage of 10 mg. If atenolol is given by infusion, 0.15mg/kg bodyweight may be administered over a 20 minute period. If required, the injection or infusion may be repeated every 12 hours. Having controlled the arrhythmias with intravenous atenolol, a suitable oral maintenance dosage is 50-100mg daily, given as a single dose.

Myocardial Infarction

Early intervention after acute myocardial infarction: For patients suitable for treatment with intravenous beta-blockade and presenting within 12 hours of the onset of chest pain, atenolol 5-10mg should be given by slow intravenous injection (1mg/minute) followed by atenolol 50mg orally about 15 minutes later, provided no

untoward effects have occurred from the intravenous dose. This should be followed by a further 50mg orally 12 hours after the intravenous dose and then 12 hours later by 100mg orally, once daily. If bradycardia and/or hypotension requiring treatment, or any other untoward effects occur, atenolol should be discontinued.

Late intervention after acute myocardial infarction: For patients who present some days after suffering an acute myocardial infarction an oral dose of atenolol (100mg daily) is recommended for long-term prophylaxis of myocardial infarction.

Elderly Dosage requirements may be reduced, especially in patients with impaired renal function.

Children There is no paediatric experience with atenolol and for this reason it is not recommended for use in children.

Renal Failure Since atenolol is excreted via the kidneys the dosage should be reduced in cases of severe impairment of renal function.

No significant accumulation of atenolol occurs in patients who have a creatinine clearance greater than 35 ml/min/1.73 m² (normal range is 100-150 ml/min/1.73 m²).

For patients with a creatinine clearance of 15-35 ml/min/1.73 m² (equivalent to serum creatinine of 300-600 micromol/litre) the oral dose should be 50 mg daily and the intravenous dose should be 10 mg once every two days.

For patients with a creatinine clearance of 600 micromol/litre) the oral dose should be 25 mg daily or 50 mg on alternate days and the intravenous dose should be 10 mg once every four days.

Patients on haemodialysis should be given 50 mg orally after each dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

4.3. Contraindications

- Hypersensitivity to the active substance, or any of the excipients listed in section 6.1.
- In patients with: uncontrolled heart failure, second or third degree heart block, bradycardia, cardiogenic shock, severe peripheral arterial circulation disturbances, hypotension, metabolic acidosis, untreated phaeochromocytoma or sick sinus syndrome.
- The administration of atenolol with a Class 1 antiarrhythmic agent, i.e. disopyramide, is contraindicated.

4.4. Special warnings and precautions for use

Although contraindicated for uncontrolled heart failure, Vascoten may be used with caution in patients whose signs of heart failure have been controlled, especial caution should be used with patients with poor cardiac reserve.

Vascoten is a beta₁ selective beta adrenoceptor blocking drug, it may be used with great caution in patients with Prinzmetal's angina, due to unopposed alpha receptor mediated coronary artery vasoconstriction it may increase the frequency and duration of angina attacks in such patients.

It can aggravate peripheral arterial circulatory disturbances that are not severe enough to be a contraindication. In patients with first degree heart block, caution must be exercised as it has a negative effect on conduction time.

Atenolol can mask the symptoms of thyrotoxicosis.

Tachycardia of hypoglycaemia may be modified.

The pharmacological action reduces heart rate, should patients develop symptoms of this, dose reduction is indicated.

Patients with ischemic heart disease should not have Vascoten discontinued suddenly.

Patients with a history of anaphylactic reactions to allergens may suffer more severe anaphylactic reactions to the allergens if on Vascoten. Such patients may be unresponsive to the usual doses of adrenaline used to treat the allergic reactions.

Unless there are compelling clinical reasons, should not be used in patients with reversible obstructive airways disease, despite having less effect on lung function than non-selective beta-adrenoceptor blocking drugs. If used, caution should be exercised. Vascoten in asthmatic patients may occasionally increase airways resistance; this is usually reversible by the commonly used dosages of broncho-dilators.

4.5. Interactions with other medicinal products and other forms of interaction

Concomitant use of beta-adrenoreceptor blockers with negative inotropic effect calcium channel blockers, such as diltiazem or verapamil, can lead to exaggeration of the effects. This happens especially in patients with impaired ventricular function and/or atrio-ventricular or sino-atrial conduction abnormalities. Neither agent should be administered within 48 hours of discontinuing the other.

The risk of hypotension is increased, and in patients with latent cardiac insufficiency cardiac failure may occur, during concomitant therapy with dihydropyridines such as nifedipine.

Following the withdrawal of clonidine, rebound hypertension can occur, this may be exacerbated by beta - adrenoceptor drugs. If the two are being concomitantly administered, Vascoten should be withdrawn several days prior to clonidine withdrawal. If replacing clonidine with Vascoten, administration should not start until several days post clonidine withdrawal.

Beta-adrenoreceptor drugs in association with digitalis glycosides may increase atrio-ventricular conduction time.

Sympathomimetic agents, i.e. adrenaline, concomitantly administered, may negate the effects of beta-adrenoreceptor blockers.

Concomitant use with insulin and oral antidiabetic drugs may lead to the intensification of the blood sugar lowering effects of these drugs. Symptoms of hypoglycaemia, particularly tachycardia, may be masked.

NSAIDs, that act as prostaglandin synthetase inhibitors, i.e., ibuprofen or indomethacin, concomitantly administered, may decrease the hypotensive effect of the beta-adrenoreceptor blockers.

Beta-adrenoreceptor blocker drugs used with anaesthesia can result in attenuation of the reflex tachycardia and increase the risk of hypotension. It is best to withdraw the beta-adrenoreceptor blocker prior to anaesthesia, but if not caution must be exercised, and the anaesthetist should be informed. Anaesthetic agents causing myocardial depression should be avoided, and an agent with the least inotropic activity possible should be chosen.

4.6. Fertility, pregnancy and lactation

Pregnancy

Atenolol crosses the placenta and appears in the cord blood. There are no studies on the use of atenolol in the first trimester; the possibility of foetal injury cannot be excluded. Atenolol has been used for the treatment of mild to moderate hypertension in the third trimester, under close supervision, but has been associated with intra-uterine growth retardation.

Use of atenolol in women who are, or may, become pregnant, especially in the first and second trimester, requires careful assessment of the clinical benefits versus the possible risks.

Breast-feeding

Atenolol accumulates in breast milk, breast feeding is not recommended, but if done, caution should be exercised.

4.7. Effects on ability to drive and use machines

The ability to drive or operate machines is unlikely to be impaired by atenolol, although dizziness or fatigue may occasionally occur.

4.8. Undesirable effects

Atenolol is well tolerated. In clinical studies, the undesired events reported are usually attributable to the pharmacological actions of atenolol.

The following undesired events, listed by body system, have been reported with the following frequencies:

- Very common ($\geq 1/10$)
- Common ($\geq 1/100$ to $< 1/10$)
- Uncommon ($\geq 1/1,000$ to $< 1/100$)
- Rare ($\geq 1/10,000$ to $< 1/1,000$)
- Very rare ($< 1/10,000$)
- Not known (cannot be estimated from the available data)

Blood and lymphatic system disorders:

Rare: Thrombocytopenia, purpura.

Psychiatric disorders:

Uncommon: Sleep disturbances,

Rare: Mood changes, confusion, psychoses and hallucinations.

Nervous system disorders:

Rare: Dizziness, headache, paresthesia.

Eye disorders:

Rare: Visual disturbances, dry eyes.

Cardiac disorders

Common: Bradycardia.

Rare: Heart failure deterioration, precipitation of heart block.

Vascular disorders:

Common: Cold extremities.

Rare: Postural hypotension which may be associated with syncope, Raynaud's phenomenon and intermittent claudication have occurred in susceptible patients.

Respiratory, thoracic and mediastinal disorders:

Rare: Patients with bronchial asthma, or a history of asthma, may suffer bronchospasm.

Gastrointestinal disorders:

Common: Gastrointestinal disturbances

Rare: Dry mouth.

Hepato-biliary disorders:

Uncommon: Elevations of transaminase levels

Rare: Hepatic toxicity, including intrahepatic cholestasis.

Skin and subcutaneous tissue disorders:

Rare: Alopecia, psoriasiform skin reactions or worsening of psoriasis, skin rashes.

General disorders and administration site condition:

Common: Fatigue

Investigations:

Very rare: An increase in anti-nuclear antibodies (ANA) has been observed, the clinical relevance is uncertain.

If any of the above are severe, or threatening the patient's well-being, consideration should be given to discontinuing the drug, on the basis of clinical judgement.

4.9. Overdose

Symptoms

These may include bradycardia, hypotension, bronchospasm and acute cardiac insufficiency.

Management

In general terms it requires close supervision and hospitalization. Drug absorption should be minimised or prevented by gastric lavage, activated charcoal slurry and a laxative. Hypotension and shock should be treated with plasma or plasma substitutes. Consideration may be given to the use of haemodialysis or haemoperfusion. Excessive bradycardia may be treated with atropine (1-2mg) via the i.v route; if necessary a bolus of 10mg glucagon i.v. may follow. The glucagon dose may be repeated if required. If there is no response to glucagon, dobutamine (2.5-10µg/kg/min) by i.v. infusion can be given. Dobutamine may also treat hypotension and acute cardiac insufficiency. In the case of a large overdose, the dobutamine dosage may need to be increased to achieve a clinical response.

Bronchodilators are usually sufficient to reverse bronchospasm.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Beta blocking agents, selective, Beta Blocking Agents; C07AB03, ATC code: C07AB03
It is a beta-adrenoceptor blocking drug which acts preferentially on beta₁-adrenergic receptors in the heart, it is beta₁-selective. Selectivity decreases with increasing dose. It has no intrinsic sympathomimetic or membrane stabilising properties and has negative inotropic effects.

The mode of action in the treatment of hypertension is unclear; in angina it is probably the effect of atenolol in reducing cardiac rate and contractility that make it effective.

5.2. Pharmacokinetic properties

Absorption

Absorption of atenolol following oral dosing is consistent but incomplete (approximately 40–50%) with peak plasma concentrations occurring 2–4 hours after dosing. The bioavailability is decreased by 20% when taken with food. There is a linear relationship between dosage and plasma concentration. The inter-subject variability in AUC and C_{max} is about 30-40%. There is no significant hepatic metabolism of atenolol and more than 90% of that absorbed reaches the systemic circulation unaltered.

Distribution

Atenolol penetrates tissues poorly due to its low lipid solubility and its concentration in brain tissue is low. The volume of distribution is 50 to 75L. The protein binding is low (approximately 3%). Most of an absorbed dose (85-100%) is excreted unchanged via the urine.

Elimination

The clearance is about 6 l/h and the half-life is about 6 to 9 hours. In elderly patients, clearance is decreased and elimination half-life increased. The clearance is correlated to renal function and the elimination is prolonged in patients with renal impairment. Impaired liver function does not influence the pharmacokinetics of atenolol.

5.3. Preclinical safety data

As atenolol is a well-established drug, and no novel pharmaceutical excipients are used in this formulation, there is no additional preclinical safety data.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Vascoten 50mg Tablet contains: Magnesium carbonate heavy, Starch, pregelatinised, Sodium laurilsulfate, Magnesium stearate, Purified water¹, Opadry white, Red iron oxide (E-172)

Vascoten 100mg Tablet contains: Magnesium carbonate heavy, Starch, pregelatinised, Sodium laurilsulfate, Magnesium stearate, Purified water¹, Opadry white

6.2. Incompatibilities

None

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store below 30°C in the original package

6.5. Nature and contents of container

PVC – PVDC film and aluminium foil blisters of ten tablets.

Packs of 20, 30, 100 and 500 tablets are available for Vascoten 50mg Tablet

Packs of 20, 30, 100, 250 and 500 tablets are available for Vascoten 100mg Tablet

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. MANUFACTURER HOLDER

[MEDOCHEMIE LTD \(Central Factory\), 1-10 Constantinoupoleos street, 3011 Limassol, Cyprus](#)

8. PRODUCT REGISTRATION HOLDER

KOMEDIC SDN BHD, 4, Jalan PJS 11/14, Bandar Sunway, 46150 Petaling Jaya, Selangor D.E.

9. DATE OF REVISION OF THE TEXT

[December 2022](#)