Atenol

DESCRIPTION:

Atenol Film Coated Tablet 50mg: White, round, convex, plain on both sides, film coated tablet.
Atenol Film Coated Tablet 100mg: 10mm Round biconvex scored on one side and plain on other side, orange-film coated tablet

COMPOSITION:

Atenol Film Coated Tablet 50mg : Each tablet contains 50mg Atenolol
Atenol Film Coated Tablet 100mg: Each tablet contains 100mg Atenolol

PHARMACODYNAMICS:

Atenolol is a beta-blocker which is beta1-selective (i.e. acts preferentially on beta-adrenergic receptors in the heart). Selectivity decreases with increasing dose.
Atenolol is without intrinsic sympathomimetic and membrane-stabilising activities and as with other beta-blockers, has negative inotropic effects (and is therefore contraindicated in uncontrolled heart failure).
As with other beta-blockers, the mode of action of atenolol in the treatment of hypertension is unclear.
It is probably the action of atenolol in reducing cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of patients with angina.
It is unlikely that any additional ancillary properties possessed by S (-) atenolol, in comparison with the racemic mixture, will give rise to different therapeutic effects.
Atenolol is effective and well-tolerated in most ethnic populations although the response may be less in black patients.
Atenolol is effective for at least 24 hours after a single oral dose. The drug facilitates compliance by its acceptability to patients and simplicity of dosing. The narrow dose range and early patient response ensure that the effect of the drug in individual patients is quickly demonstrated. Atenolol is compatible with diuretics, other hypotensive agents and antianginal agents (see *Interactions*). Since it acts preferentially on beta-receptors in the heart, Atenolol may, with care, be used successfully in the treatment of patients with respiratory disease, who cannot tolerate non-selective beta-blockers.
Early intervention with Atenolol in acute myocardial infarction reduces infarct size and decreases morbidity and mortality. Fewer patients with a threatened infarction progress to frank infarction; the incidence of ventricular arrhythmias is decreased and marked pain relief may result in reduced need of opiate analgesics. Early mortality is decreased. Atenolol is an additional treatment to standard coronary care.

PHARMACOKINETICS:

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 atenolol blood levels are consistent and subject to little variability. 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. Plasma protein binding is low (approximately 3%).

Elimination

The plasma half-life is about 6 hours but this may rise in severe renal impairment since the kidney is the major route of elimination.

INDICATION:

Therapeutic indications
i) Hypertension
ii) Angina pectoris
iii) Cardiac arrhythmias
iv) Myocardial infarction– Early and late intervention

RECOMMENDED DOSAGE:

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 100mg daily given orally as a single dose. Some patients, however, will respond to 50mg 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 Atenol with other antihypertensive agents. For example, co-administration of Atenol with a diuretic, provides a highly effective and convenient antihypertensive therapy.

Angina

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

Cardiac Arrhythmias

A suitable initial dose of Atenol 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 10mg. If Atenol 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 Atenol, a suitable oral maintenance dosage is 50-100mg daily, given as a single dose.

Myocardial Infarction

For patients suitable for treatment with intravenous beta-blockade and presenting within 12 hours of the onset of chest pain, Atenol 5-10mg should be given by slow intravenous injection (1mg/minute) followed by Atenol 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, Atenol should be discontinued.

Elderly

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

Paediatric population

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

Renal impairment

Since Atenol is excreted via kidneys the dosage should be adjusted in cases severe impairment of renal function. No significant accumulation of Atenol occurs in patients who have creatinine clearance greater than 35 mL/min/1.73m^2 (normal range is 100-150 mL/min/1.73m^2).

For patients with creatinine clearance of 15-35 mL/min/1.73m^2 (equivalent to serum creatinine of 300-600 micromol/litre) the oral dose should be 50mg daily and the intravenous dose should be 10mg once every two days.

For patients with a creatinine clearance of <15mL/min/1.73m^2 (equivalent to serum creatinine of >600 micromol/litre) the oral dose should be 25mg daily or 50mg 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.

ROUTE OF ADMINISTRATION: For administration by the oral route

CONTRAINDICATIONS:

Atenol, as with other beta-blockers, should not be used in patients with any of the following: known hypersensitivity to the active substance, or any of the excipients; bradycardia (<45bpm); cardiogenic shock; hypotension; metabolic acidosis; severe peripheral arterial circulatory disturbances; second or third degree heart block; sick sinus syndrome; untreated pheochromocytoma; uncontrolled heart failure.

WARNINGS & PRECAUTIONS:

Atenol as with other beta-blockers:

- Should not be withdrawn abruptly. The dosage should be withdrawn gradually over a period of 7-14 days, to facilitate a reduction in beta-blocker dosage. Patients should be followed during withdrawal, especially those with ischaemic heart disease.
- When a patient is scheduled for surgery, and a decision is made to discontinue beta-blocker therapy, this should be done at least 24 hours prior to the procedure. The risk-benefit assessment of stopping beta-blockade should be made for each patient. If treatment is continued, an anaesthetic with little negative inotropic activity should be selected to minimise the risk of myocardial depression. The patient may be protected against vagal reactions by intravenous administration of atropine.
- Although contraindicated in uncontrolled heart failure (see Contraindications), may be used in patients whose signs of heart failure have been controlled. Caution must be exercised in patients whose cardiac reserve is poor.
- May increase the number and duration of angina attacks in patients with Prinzmetal's angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. Atenol is a beta1-selective beta-blocker, consequently, its use may be considered although utmost caution must be exercised.
- Although contraindicated in severe peripheral arterial circulatory disturbances (see Contraindications) may also aggravate less severe peripheral arterial circulatory disturbances.
- Due to its negative effect on conduction time, caution must be exercised if it is given to patients with first degree heart block.
- May mask the symptoms of hypoglycaemia, in particular, tachycardia.
- May mask the signs of thyrotoxicosis.
- Will reduce heart rate, as a result of its pharmacological action. In the rare instance when a treated patient develops symptoms which may be attributable to a slow heart rate and the pulse rate drops to less than 50-55 bpm at rest, the dose should be reduced.
- May cause a more severe reaction to a variety of allergens when given to patients with a history of anaphylactic reactions to such allergens. Such patients may be unresponsive to the usual doses of adrenaline (epinephrine) used to treat the allergic reactions.
- May cause a hypersensitivity reaction including angioedema and urticaria.
- Should be used with caution in the elderly, starting with a lesser dose (Posology and method of administration)

Since Atenol is excreted via kidneys, dosage should be reduced in patients with creatinine clearance of below 35 mL/min/1.73m^2.

Although cardioselective (beta$_1$) beta-blockers may have less effect on lung function than non-selective beta-blockers, as with all beta-blockers, these should be avoided in patients with reversible obstructive airways disease, unless there are compelling clinical reasons for their use. Occasionally, some increase in airways resistance may occur in asthmatic patients however, and this may usually be reversed by commonly used dosage of bronchodilators such as salbutamol or isoprenaline.

As with other beta-blockers, in patients with a pheochromocytoma, an alpha-blocker should be given concomitantly.

INTERACTION WITH OTHER MEDICAMENTS:

Combined use of beta-blockers are calcium channel blockers with negative inotropic effects e.g verapamil, diltiazem can lead to an exaggeration of these effects particularly in patients with impaired ventricular function and/or sinoatrial or atrioventricular conduction abnormalities. This may result in severe hypotension, bradycardia and cardiac failure. Neither the beta-blocker nor the calcium channel blocker should be administered intravenously within 48 hours of discontinuing the other.

Concomitant therapy with dihydropyridines e.g. nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency.

Digitalis glycosides, in association with beta-blockers, may increase atrioventricular conduction time.

Beta-blockers may exacerbate the rebound hypertension, which can follow the withdrawal of clonidine. If the two drugs are co-administered, the beta-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine administration by beta-blocker therapy, the introduction of beta-blockers should be delayed for several days after clonidine administration has stopped. (See also prescribing information for clonidine).

Class 1 anti-arrhythmic drugs (e.g. disopyramide) and amiodarone may have a potentiating effect on atrial-conduction time and induce negative inotropic effect.
Concomitant use of sympathomimetic agents, e.g. adrenaline (epinephrine), may counteract the effect of beta-blockers.

Concomitant use of 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 (see Special warnings and precautions for use).

Concomitant use of prostaglandin synthase inhibiting drugs (e.g. ibuprofen, indomethacin), may decrease the hypotensive effects of beta-blockers.
Caution must be exercised when using anaesthetic agents with Atenolol. Thus anaesthetist should be informed and the choice of anaesthetic should be an agent with as little negative inotropic activity as possible. Use of beta-blockers with anaesthetic drugs may results in attenuation of the reflux tachycardia and increase the risk of hypotension. Anaesthetic agents causing myocardial depression are best avoided.

USE IN PREGNANCY & LACTATION:
Caution should be exercised when Atenolol is administered during pregnancy or to a woman who is breast-feeding.

Use in Pregnancy:
Pregnancy
Atenolol crosses the placental barrier and appears in the cord blood. No studies have been performed on the use of Atenolol in the first trimester and the possibility of foetal injury cannot be excluded. Atenolol has been used under close supervision for the treatment of hypertension in the third trimester. Administration of Atenolol to pregnant women in the management of mild to moderate hypertension has been associated with intra-uterine growth retardation. The use of Atenolol in women who are, or may become, pregnant requires that the anticipated benefit be weighed against the possible risks, particularly in the first and second trimesters, since beta-blockers, in general, have been associated with a decrease in placental perfusion which may result in intra-uterine deaths, immature and premature deliveries.

Use in Lactation:
There is significant accumulation of Atenolol in breast milk.
Neonates born to mothers who are receiving Atenolol at parturition or breast-feeding may be at risk for hypoglycaemia and bradycardia

SIDE 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, common uncommon, rare, very rare, including isolated reports, not known (cannot be estimated from the available data).

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, intermittent claudication may be increased if already present, in susceptible patients Raynaud's phenomenon.
Respiratory, thoracic and mediastinal disorders
Rare: Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints.
Nervous system disorders:
Rare: Dizziness, headache, paraesthesia.
Psychiatric disorders:
Uncommon: Sleep disturbances of the type noted with other beta blockers
Rare: Mood changes, nightmares, confusion, psychoses and hallucinations.
Gastrointestinal disorders:
Common: Gastrointestinal disturbances.
Rare: Dry mouth
Investigations:
Uncommon Elevations of transaminase levels
Very rare: An increase in ANA (Antinuclear Antibodies) has been observed, however the clinical relevance of this is not clear.
Hepatobiliary disorders:
Uncommon: Elevations of transaminase levels
Rare: Hepatic toxicity including intrahepatic cholestasis
Blood and lymphatic system disorders:
Rare: Purpura, thrombocytopenia
Skin and subcutaneous tissue disorders:
Rare: Alopecia, psoriasiform skin reactions, exacerbation of psoriasis, skin rashes
Not Known: Hypersensitivity reactions, including angioedema and urticaria
Musculoskeletal and connective tissue disorders

Not Known: Lupus-like syndrome
Eye disorders:
Rare: Dry eyes, visual disturbances
Reproductive system and breast disorders:
Rare: Impotence
General disorders and administration site conditions:
Common: Fatigue

Discontinuance of the drug should be considered it, according to clinical judgement, the well-being of the patient is adversely effected by any of the above reactions.

SYMPTOMS AND TREATMENT OF OVERDOSE:

The symptoms of overdosage may include bradycardia, hypotension, acute cardiac insufficiency and bronchospasm.
General treatment should include: close supervision; treatment in an intensive care ward; the use of gastric lavage; activated charcoal and a laxative to prevent absorption of any drug still present in the gastrointestinal tract; the use of plasma or plasma substitutes to treat hypotension and shock. The possible uses of haemodialysis or haemoperfusion may be considered.

Excessive bradycardia can be countered with atropine 1-2mg intravenously and/or a cardiac pacemaker. If necessary, this may be followed by a bolus dose of glucagon 10mg intravenously. If required, this may be repeated or followed by an intravenous infusion of glucagon 1-10mg/hour depending on response. If no response to glucagon occurs or if glucagon is unavailable, a beta-adrenoceptor stimulant such as dobutamine 2.5 to 10 micrograms/kg/minute by intravenous infusion may be given. Dobutamine, because of its positive inotropic effect could also be used to treat hypotension and acute cardiac insufficiency. It is likely that these doses would be inadequate to reverse the cardiac effects of beta-blocker blockade, if a large overdose has been taken. The dose of dobutamine should therefore be increased if necessary to achieve the required response according to the clinical condition of the patient.
Bronchospasm can usually be reversed by bronchodilators.

STORAGE CONDITIONS:
Store in a dry place below 30°C and protected from direct sunlight.
Keep out of reach of children.
Jauhkan daripada kanak-kanak.

SHELF LIFE:
Please refer to outer package.

PACK SIZE:
Atenol Film Coated Tablet 50mg: Blister packs of 10 x 10's
Atenol Film Coated Tablet 100mg: Blister packs of 10 x 10's

PRODUCT REGISTRATION HOLDER & MANUFACTURER:
DUOPHARMA (M) SDN BHD
Lot 2599, Jalan Seruling 59 Kawasan 3,
Taman Klang Jaya, 41200 Klang, Selangor, MALAYSIA.

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