SCHEDULING STATUS: S3

PROPRIETARY NAME AND DOSAGE FORM:

GULF ATENOLOL 50 (tablets)

GULF ATENOLOL 100 (tablets)

COMPOSITION:

GULF ATENOLOL 50: Each film-coated tablet contains 50 mg of atenolol.

GULF ATENOLOL 100: Each film-coated tablet contains 100 mg of atenolol.

PHARMACOLOGICAL CLASSIFICATION:

A 5.2 Adrenolytics (Sympatholytics).

PHARMACLOGICAL ACTION:

Atenolol is a selective $ß_1$ – adrenoceptor antagonist. Beta-1 receptors are found primarily in the heart thus blockade of these receptors results in a reduction in heart rate, myocardial contractility, conduction rate of impulses and suppression of adrenergic-induced renin release.

Pharmacokinetics:

Atenolol is well absorbed following oral administration with a resultant bioavailability of about 50%. Peak plasma concentration is reached 2 to 4 hours after administration. Atenolol has low lipid solubility and thus has poor tissue penetration with low brain tissue concentrations. Protein binding is minimal. Atenolol undergoes little or no hepatic metabolism and is excreted mainly in the urine.

INDICATIONS:

GULF ATENOLOL is indicated in the management of angina pectoris and mild to moderate hypertension.

CONTRA INDICATIONS:

- Hypersensitivity to atenolol or to any of the ingredients
- Second and third degree heart block
- Bradycardia less than 50 beats/minute
- Metabolic acidosis
- Severe peripheral arterial circulatory disturbances
- Sick sinus syndrome

- Untreated phaeochromocytoma
- Hypotension

Avoid the use of GULF ATENOLOL in cardiac failure unless or until signs of failure are controlled with digitalis or diuretics.

WARNINGS:

Safety and efficacy in children have not been established.

GULF ATENOLOL should be used with caution in patients with:

- Thyrotoxicosis: symptoms may be masked
- First degree heart block – negative inotropic effects
- Asthma, bronchitis, chronic pulmonary disease
- Tachycardic responses may be obscured. Particular caution should be taken in this regard.
- Angina attacks: Patients with Prinzmetal's angina may experience an increase in the number and duration of angina attacks due to unopposed alpha receptor mediated coronary artery vasoconstriction.
- Peripheral arterial circulatory disturbances and less severe peripheral vascular diseases: peripheral circulation may be reduced resulting in a worsening of these conditions.

GULF ATENOLOL modifies the tachycardia associated with hypoglycaemia.

Patients with phaeochromocytoma require treatment with an alpha adrenergic blocker.

If the decision is made to withdraw GULF ATENOLOL before anaesthesia, at least 48 hours should be allowed to elapse between the last dose and surgery. If the medicine is to be continued, care should be taken when using anaesthetics such as ether, cyclopropane and trichloroethylene. Atropine (1-2 mg IV) may be used to correct vagal dominance. The patient must be maintained on their usual dosage perioperatively to avoid aggravation of angina pectoris or hypertension.

The dosage of GULF ATENOLOL should be adjusted in severe renal impairment (see **Dosage and Directions for Use**)

Care should be taken in prescribing GULF ATENOLOL together with Class 1 anti-dysrhythmic agents such as disopyramide, myocardial depressants and inhibitors of AV conduction such as calcium antagonists.

Caution should be exercised when transferring a patient from clonidine, as the withdrawal of clonidine may result in the release of large amounts of catecholamines that may give rise to a hypertensive crisis. If GULF ATENOLOL is administered in these circumstances, the unopposed alpha-receptor stimulation may potentiate this effect. If GULF ATENOLOL and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of GULF ATENOLOL as severe rebound hypertension may occur.

GULF ATENOLOL should be used with caution in combination with verapamil in patients with impaired ventricular function. This combination should not be given to patients with conduction abnormalities. Neither medication should be administered intravenously within 48 hours of discontinuing the other. The intravenous administration of calcium antagonists and anti-dysrhythmic agents is not recommended during therapy with GULF ATENOLOL.

INTERACTIONS:

Care should be taken when using anaesthetic agents with GULF ATENOLOL. The anaesthetist should be informed and the choice of anaesthetic should be an agent with as little negative inotropic activity as possible. Use of GULF ATENOLOL with anaesthetic agents may result in attenuation of the reflex tachycardia and increase the risk of hypotension. Anaesthetic agents causing myocardial depression are best avoided.

Concomitant use of GULF ATENOLOL with:

- Phenothiazines: each medication appears to inhibit the metabolism of the other resulting in increased levels of both medicines. This interaction may have life threatening consequences.
- Quinidine, procainamide, lignocaine: myocardial depressant effects may be enhanced by GULF ATENOLOL.
- Hypoglycaemic agents: hypoglycaemic effects may be enhanced. This interaction may have life threatening consequences.
- Clonidine: rebound hypertension can occur with concomitant use, especially following sudden withdrawal of GULF ATENOLOL. If GULF ATENOLOL and clonidine are used together, then clonidine should not be discontinued until several days after the withdrawal of the beta blocker.

- Disopyramide: since both medicines can cause depressed contractility and conductivity of the heart, severe bradycardia is possible. This medicine – medicine interaction may have life threatening consequences.
- Calcium blockers: concurrent use may result in severe hypotension and cardiac failure may occur in patients with latent cardiac insufficiency.
- Verapamil: use with caution in patients with impaired ventricular function and/ or SA or AV conduction abnormalities. This combination should not be given to patients with conduction abnormalities.
- Sympathomimetics such as adrenaline/ epinephrine: may negate the effect of GULF ATENOLOL.

Non-steroidal anti-inflammatory medicines (e.g. indomethacin and ibuprofen) – may decrease the hypotensive effect of beta blockers.

PREGNANCY AND LACTATION:

Safety and efficacy in pregnancy and lactation have not been established.

Administration of GULF ATENOLOL to pregnant mothers has been associated with growth retardation of the foetus. Administration of GULF ATENOLOL to pregnant mothers shortly before birth or during labour may result in hypotonia, collapse or hypoglycaemia in the newborn.

DOSAGE AND DIRECTIONS FOR USE:

Children:

Safety and efficacy have not been established.

Adults:

Angina Pectoris

50 to 100 mg daily as single or divided doses

Hypertension

50 to 100 mg daily as a single dose

Additional doses are unlikely to be of any benefit.

GULF ATENOLOL may be combined with diuretics or other antihypertensive agents to achieve a further reduction in blood pressure.

Elderly:

May have increased or decreased sensitivity to the effects of the usual adult dose and a dose reduction may be necessary.

The usual dose for both indications is 50 mg once daily.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Blood and Lymphatic System Disorders:

Less frequent – thrombocytopenia, purpura

Psychiatric Disorders:

Less frequent – Sleep disturbances of the type noted with other beta-blockers, hallucinations, psychosis, mood changes, nightmares, confusion, depression

Nervous System Disorders:

Less frequent – Dizziness, headache, paraesthesia, restlessness

Gastrointestinal Disorders:

Frequent – Gastrointestinal disturbances, nausea, vomiting, diarrhoea, constipation

Less frequent – Dry mouth, mass gain, stomatitis

Hepatobiliary Disorders:

Less frequent – Elevations of transaminase levels, hepatic toxicity including intrahepatic cholestasis

Musculoskeletal, connective tissue and bone disorders:

Less frequent – muscle cramps, myopathy, skeletal muscle weakness

General Disorders and Administration Site Conditions:

Frequent – Fatigue

Eye Disorders:

Less frequent – Dry eyes, visual disturbances

Ear and labyrinth disorders:

Less frequent – transient hearing loss

Cardiac Disorders:

Frequent – Bradycardia

Less frequent – Heart failure deterioration, precipitation of heart block

Vascular Disorders:

Frequent – Cold extremities

Less frequent – Postural hypotension which may be associated with syncope, hypertension, intermittent claudication may be increased if already present, in susceptible patients presenting with Raynaud's phenomenon, peripheral gangrene may be precipitated

Respiratory, Thoracic and Mediastinal Disorders:

Less frequent – Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints

Skin and Subcutaneous Tissue Disorders:

Less frequent – alopecia, psoriasiform skin reactions, exacerbation of psoriasis, skin rashes, perspiration

Frequency not known – Hypersensitivity reactions, including angioedema and urticaria

Reproductive System and Breast Disorders:

Less frequent – Impotence

Investigations:

Less frequent – An increase in anti-nuclear antibodies (ANA) has been observed, however the clinical relevance of this is not clear.

Adverse reactions are common with patients with renal decomposition.

Special Precautions

Abrupt discontinuation of treatment may cause exacerbation of angina pectoris inpatients suffering from ischaemic heart disease. Discontinuation of therapy should be gradual, and patients should be advised to limit the extent of their physical activity during the period that the medicine is being discontinued.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(See Side Effects and Special Precautions)

Overdosage may produce bradycardia and severe hypotension. Bronchospasm and heart failure may be produced in certain individuals.

Cases of overdose should be observed for at least 4 hours, as apnoea and cardiovascular collapse may appear suddenly.

Repeated administration of activated charcoal may be necessary in overdose.

Atropine may be used to treat severe bradycardia. If the response is inadequate, glucagon may be given

intravenously. Alternatively, dobutamine may be required to reverse beta-blockade. Cardiac pacing may be required for severe bradycardia. Bronchospasm should be treated with intravenous aminophylline or inhaled or intravenous beta-agonist, e.g. salbutamol.

IDENTIFICATION:

GULF ATENOLOL 50: White, round, biconvex, film coated tablets with central break-line on one side

GULF ATENOLOL 100: Orange, round, biconvex, film coated tablets with central break-line on one side

PRESENTATION:

Patient ready packs of 28 tablets

Unit carton containing 28 or 30 tablets in clear PVC/silver printed aluminium blister packs

White HDPE containers of 30, 100, 500 or 1000 tablets

STORAGE INSTRUCTIONS:

Store at or below 25 °C in a cool, dry place. Do not remove tablets from unit cartons until required for use.

Protect from light and moisture. Keep HDPE containers tightly closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

Gulf Atenolol 100 – 41/5.2/0004

Gulf Atenolol 50 – 41/5.2/0005

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Gulf Drug Company (Pty) Ltd

22 Burnside Drive

Old Mill Industrial Park

Mount Edgecombe, 4300

www.gulfdrug.co.za

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

19/03/2010