1.3.1.1. PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

TENCHLOR 100 mg/ 25 mg film-coated tablets

TENCHLOR HS 50 mg/ 12,5 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TENCHLOR

Each film-coated tablet of TENCHLOR contains 100 mg of atenolol and 25 mg of chlorthalidone.

Contains sugar: Lactose monohydrate 228 mg

TENCHLOR HS

Each film-coated tablet of TENCHLOR HS contains 50 mg of atenolol and 12,5 mg of chlorthalidone.

Contains sugar: Lactose monohydrate 114 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets

TENCHLOR is a white to cream biconvex film-coated tablet, bisected on one side and

engraved with the word “TENCHLOR” on the other side.

TENCHLOR HS is a white, to cream, biconvex, film-coated tablet, bisected on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TENCHLOR is indicated for:

- The management of mild to moderate hypertension.

4.2 Posology and method of administration

Posology

Adults

TENCHLOR: Half to one tablet daily in the morning.

TENCHLOR HS: One to two tablets daily in the morning.

There is little or no further fall in blood pressure with increased dosage.

Patients should be warned not to stop taking the medicine except on the advice of their medical doctor and the importance of compliance with therapy should be stressed.

Patients should be advised not to take other medicines without professional advice.

Special populations

Elderly population

TENCHLOR should not be used in elderly patients, without reducing the normal dose (see section 4.3).

Renal impairment

TENCHLOR should not be given to patients with severe renal impairment or anuria (see section 4.3).

Hepatic impairment

TENCHLOR should be avoided in patients with severe hepatic impairment, in whom encephalopathy may be precipitated (see section 4.3).

Paediatric population

TENCHLOR is not recommended for children.

Method of administration

For oral administration.

4.3 Contraindications

TENCHLOR is contraindicated in:

- Patients with hypersensitivity to atenolol and chlorthalidone or any excipients in TENCHLOR (see section 6.1).
- Patients with partial heart block, heart failure, metabolic acidosis or sinus bradycardia, and should never be given to patients with untreated phaeochromocytoma without concomitant alpha-adrenoceptor blocking therapy.
- Patients taking verapamil concomittently, neither medicine should be administered within several days of discontinuing the other.
- Patients with bronchial asthma, bronchitis, bronchospasm or chronic respiratory diseases,

atrioventricular block, marked bradycardia (less than 50 beats per minute), heart failure refractory to digitalis, uraemia, hypoglycaemia, second and third degree heart block, peripheral vascular diseases and Raynaud's phenomenon.

- Patients with severe hepatic impairment, in whom encephalopathy may be precipitated.
- Pregnancy and lactation.
- Elderly patients, or in patients suffering from renal dysfunction without reducing the normal dose of TENCHLOR.
- Patients with severe renal impairment or anuria.
- Patients with Addison's disease.
- Patients in the peri-operative period, it is generally unwise to reduce the dosage to that which the patient is accustomed, as there may be danger of aggravation of angina pectoris or of hypertension.
- A patient's normal tachycardiac response to hypo-volaemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard.
- Patients with pre-existing hypercalcaemia.
- Cardiogenic shock.
- Hypotension.
- Sick sinus syndrome.
- Severe renal failure.
- Uncontrolled heart failure.
- Patients with metabolic acidosis (e.g. in diabetes) and after prolonged fasting.

4.4 Special warnings and precautions for use

TENCHLOR should be given to patients with congestive heart failure only when they are fully digitalised and only then with great caution. Great care should be exercised when giving TENCHLOR to patients undergoing general anaesthesia, and myocardial depressants, such as

chloroform and ether must be avoided.

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

TENCHLOR should be used with caution in patients with impaired hepatic or renal function or adrenal disease (see section 4.3).

Due to its beta-blocker component in TENCHLOR tablets:

-Atenolol as contained in TENCHLOR may mask the symptoms of hyperthyroidism. It may also mask the symptoms of hypoglycaemia, as well as enhance the effects of hypoglycaemic medicines in patients with diabetes mellitus.

-Beta blockers may unmask myasthenia gravis.

-Special precaution must be taken in patients with psoriasis, as this may be aggravated.

-Patients with a history of anaphylaxis to an antigen may be more reactive to repeated challenge with the antigen while taking atenolol, as in TENCHLOR.

-The dose may need to be reduced in patients with renal or hepatic dysfunction.

Important:

-Digitalisation of patients receiving long-term beta-blocker therapy may be necessary if congestive heart failure is likely to develop. This combination can be considered despite the

potentiation of negative chronotropic effects of the two medicines. Careful control of dosages and of the individual patient's response (and notably pulse-rate) is essential in this situation.

-Abrupt withdrawal of therapy has sometimes resulted in angina, myocardial infarction, ventricular dysrhythmias and death. Discontinuation of therapy should be gradual (1 to 2 weeks) and patients should be advised to limit the extent of their physical activity during the period that the medicine is being discontinued.

- Although contraindicated in uncontrolled heart failure (see section 4.3) it 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. Atenolol, as in TENCHLOR, is a $beta_1$-selective beta-blocker; consequently the use of TENCHLOR tablets may be considered although utmost caution must be exercised.

- Although contraindicated in severe peripheral arterial circulatory disturbances (see section 4.3) it 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 modify warning signs of hypoglycaemia such as tachycardia, palpitation and sweating.

- May mask the cardiovascular signs of thyrotoxicosis.

- Will reduce heart rate, as a result of its pharmacological action. In the rare instances when a treated patient develops symptoms which may be attributable to a slow heart rate, the dose may be reduced.

- Should not be discontinued abruptly in patients suffering from ischaemic heart disease.

- May cause a more severe reaction to a variety of allergens, when given to patients with a history of anaphylactic reaction to such allergens. Such patients may be unresponsive to the usual doses of adrenaline used to treat the allergic reactions.

- May cause a hypersensitivity reaction including angioedema and urticaria (see section 4.8).

- Patients with bronchospastic disease should, in general, not receive beta-blockers due to an increase in airways resistance. Atenolol, as in TENCHLOR, is a $beta_1$-selective beta-blocker; however this selectivity is not absolute. Therefore the lowest possible dose of TENCHLOR tablets should be used and utmost caution must be exercised. If increased airways resistance does occur, TENCHLOR tablets should be discontinued and bronchodilator therapy (e.g. salbutamol) administered if necessary.

The label and patient information leaflet for this medicine state the following warning:

“**If you have ever had asthma or wheezing, do not take this medicine without first checking with your healthcare professional”.**

- Systemic effects of oral beta-blockers may be potentiated when used concomitantly with ophthalmic beta-blockers.

- In patients with phaeochromocytoma it must be administered only after alfa-receptor blockade. Blood pressure should be monitored closely.

- Caution must be exercised when using anaesthetic medicines with TENCHLOR tablets. The anaesthetist should be informed and the choice of anaesthetic should be a medicine with as little negative inotropic activity as possible. Use of beta-blockers with anaesthetic medicines may result in attenuation of the reflex tachycardia and increase the risk of hypotension. Anaesthetic medicines causing myocardial depression are best avoided.

Chlorthalidone

Due to its chlorthalidone component:

– Chlorthalidone as contained in TENCHLOR may cause hypokalaemia which intensifies the effect of digitalis on cardiac muscle and administration of digitalis or its glycosides may have to be temporarily suspended. Patients with severe coronary artery disease and cirrhosis of the liver are particularly at risk from hypokalaemia. Hyponatraemia may occur in patients with severe congestive heart failure who are very oedematous, particularly with large doses in conjunction with restricted salt in the diet.

- Plasma electrolytes should be periodically determined in appropriate intervals to detect possible electrolyte imbalance especially hypokalaemia and hyponatraemia.

- Hypokalaemia and hyponatraemia may occur. Measurement of electrolytes is recommended, especially in the older patient, those receiving digitalis preparations for cardiac failure, those taking an abnormal (low in potassium) diet or those suffering from gastrointestinal complaints. Hypokalaemia may predispose to dyshythmias in patients receiving digitalis.

- Impaired glucose tolerance may occur and diabetic patients should be aware of the potential for increased glucose levels. Close monitoring of glycaemia is recommended in the initial phase of therapy and in prolonged therapy testing for glucosuria should be carried out at regular intervals.

-There is an increased risk of patients taking chlorthalidone as contained in TENCHLOR developing cholecystitis.

-Chlorthalidone as contained in TENCHLOR should be used with caution in patients with impaired hepatic function since it may increase the risk of hepatic encephalopathy. It should also be given with caution in renal impairment since it can further reduce renal function. It may precipitate attacks of gout in susceptible patients. All patients should be carefully observed for signs of fluid and electrolyte imbalance, especially in the presence of vomiting or during parenteral fluid therapy. Chlorthalidone as contained in TENCHLOR may exacerbate or activate systemic lupus erythematosus in susceptible patients.
-In patients with impaired hepatic function or progressive liver disease, minor alterations in fluid and electrolyte balance may precipitate hepatic coma.

- Hyperuricaemia may occur. Only a minor increase in serum uric acid usually occurs but in cases of prolonged elevation, the concurrent use of a uricosuric medicine will reverse the hyperuricaemia.

Choroidal effusion, acute myopia and secondary angle-closure glaucoma:

-Sulfonamide or sulfonamide derivative medicines can cause an idiosyncratic reaction resulting in choroidal effusion with visual field defect, transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of medicine initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue medicine intake as rapidly as possible. Prompt medical or surgical treatments may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

Paediatric population

The use of TENCHLOR is not recommended in children. The safety and efficacy of TENCHLOR in children has not yet been established.

Excipients

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Due to atenolol

Carbohydrate and lipid metabolism

Atenolol as contained in TENCHLOR interferes with carbohydrate and lipid metabolism and can produce hypoglycaemia, hyperglycaemia and changes in blood concentrations of triglycerides and cholesterol.

Both pharmacodynamic and pharmacokinetic interactions have been reported with beta-blockers. Pharmacodynamic interactions may occur with medicines whose actions enhance or antagonise the various effects of beta-blockers at $beta_1$ and $beta_2$ receptors.

Interactions may occur with medicines that interfere with the antihypertensive effect, cardiodepressant effect, effect on carbohydrate metabolism, or effect on bronchial $beta_2$ receptors of beta-blockers. Medicines that enhance the antihypertensive effects of beta-blockers, such as ACE inhibitors, calcium-channel blockers, and clonidine (see section 4.4) may be useful in controlling hypertension.

Aldesleukin and general anaesthetics

Medicines that cause hypotension such as aldesleukin and general anaesthetics also enhance the antihypertensive effects of beta-blockers while other medicines, for example nonsteriodal anti-inflammatories antagonise the antihypertensive effects.

If beta-blockers are not discontinued prior to anaesthesia, a medicine such as atropine may be given to counter increases in vagal tone.

Anaesthetics that cause myocardial depression, such as ether, cyclopropane, and trichloroethylene are best avoided. Awareness by the anaesthetist that beta-blockers are being taken is of the greatest importance.

Cardiac depressants

Concomitant use of beta-blockers with other cardiac depressants such as amiodarone, diltiazem, and verapamil can precipitate bradycardia and heart block. Concurrent administration of calcium-channel blockers and beta-blockers has resulted in hypotension, bradycardia, conduction defects and cardiac failure.

Sotalol

Sotalol is particularly prone to interactions with other medicines affecting cardiac conduction.

Myocardial depressants

The effects of other myocardial depressants, including anti-dysrhythmics such as quinidine, procainamide, or lignocaine, phenytoin, and medicines which interfere with calcium transport, such as verapamil, may also be enhanced by atenolol as contained in TENCHLOR. Class I anti-dysrhythmic medicines (e.g. disopyramide) and amiodarone may have a potentiating effect on atrial-conduction time and induce negative inotropic effect.

An enhanced antihypertensive effect is seen when other antihypertensives are given concomitantly.

Prazosin

Beta-blockers can potentiate the severe postural hypotension that may follow the initial dose of prazosin and can exacerbate rebound hypertension following withdrawal of clonidine treatment. If the two medicines are co-administered, the beta-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine by beta-blocker therapy, the introduction of beta-blockers should be delayed for several days after clonidine administration has stopped.

Beta-adrenoceptor stimulating medicines

The effects of atenolol as contained in TENCHLOR are diminished by beta-adrenoceptor stimulating medicines such as isoprenaline; the hypotensive effects of atenolol as contained in TENCHLOR may be dangerously reversed and the peripheral vasoconstrictor effects enhanced by alpha-adrenoceptor stimulating medicines such as noradrenaline or those with mixed alpha- and beta-adrenoceptor stimulating properties such as adrenaline; bradycardia may also occur.

Adrenergic neurone blocking medicines

The effects of atenolol may be enhanced by adrenergic neurone blocking medicines such as guanethidine or bethanidine, or catecholamine-depleting medicines such as reserpine, and the hypotensive effects by diuretics.

Digitalis

Atenolol as contained in TENCHLOR may enhance some of the cardiac effects of digitalis and diminish others. Digitalis glycosides, in association with beta-blockers, may increase atrio-ventricular conduction time. Beta-blockers may potentiate bradycardia due to digoxin.

Clonidine

It has been suggested that clonidine withdrawal symptoms may be exacerbated in patients who are concurrently taking a beta-blocker.

In diabetic patients, beta-blockers can reduce the response to insulin and oral hypoglycaemics through their effects on pancreatic beta receptors.

Sympathomimetics

Blockade of peripheral beta receptors interferes with the effects of sympathomimetics; patients on beta-blockers, especially non-selective beta-blockers, may develop elevated blood pressure if they are given adrenaline.

Adrenaline

The bronchodilator effects of adrenaline are also inhibited. The response to adrenaline given for anaphylaxis may be reduced in patients on long-term treatment with beta blockers.

Pharmacokinetic interactions occur with medicines that alter the absorption or metabolism of beta-blockers.

Aluminium salts

Medicines that reduce absorption include aluminium salts, and bile-acid binding resins such as colestyramine.

Barbiturates

Metabolism of beta-blockers can be increased by concomitant treatment with medicines such as barbiturates and rifampicin and decreased with medicines such as cimetidine, erythromycin, fluvoxamine, and hydralazine.

Hepatic blood flow

Medicines that alter hepatic blood flow also affect metabolism of beta-blockers, e.g. cimetidine and hydralazine decreases hepatic blood flow and this contributes to the decreased hepatic clearance seen with these medicines.

Hepatic metabolism

Medicines that influence hepatic metabolism affect beta-blockers, such as labetalol, propranolol and timolol, that are extensively metabolised while beta-blockers that are excreted largely unchanged, eg. atenolol and nadolol, are unaffected.

Ampicillin

Serum-atenolol concentrations were reduced by concurrent administration of ampicillin given in doses of 1 gram per mouth.

Prostagladin synthetase

Concomitant use of prostaglandin synthetase inhibiting medicines (e.g. ibuprofen, indometacin) may decrease the hypotensive effects of beta-blockers.

Please note: Such interactions can have life-threatening consequences.

Due to chlorthalidone

Digitalis glycosides

Many of the interactions of chlorthalidone as contained in TENCHLOR is due to the effects on fluid and electrolyte balance. Diuretic-induced hypokalaemia may enhance the toxicity of digitalis glycosides by depleting serum-potassium concentrations and may also increase the risk of dysrhythmias with medicines such as astemizole, terfenadine, halofantrine, pimozide, and sotalol.

Muscle relaxants

It may enhance the neuromuscular blocking action of competitive muscle relaxants, such as tubocurarine probably by the hypokalaemic effect.

Other antihypertensive medicines

It may enhance the effect of other antihypertensive medicines, particularly the first-dose hypotension that occurs with alpha-blockers or angiotensin converting enzyme inhibitors, while postural hypotension associated with chlorthalidone therapy may be enhanced by concomitant ingestion of alcohol, barbiturates, or opioids.

Corticosteroids

The potassium-depleting effect of chlorthalidone as contained in TENCHLOR may be enhanced by corticosteroids, corticotrophin, beta$_2$ agonists such as salbutamol, carbenoxolone, or amphotericin.

Diuretics

The antihypertensive effects of diuretics may be antagonised by medicines that cause fluid retention, such as corticosteroids, nonsteroidal anti-inflammatories, or carbenoxolone.

Lithium

Concomitant administration of chlorthalidone as contained in TENCHLOR and lithium is not generally recommended as the association may lead to toxic blood concentrations of lithium. The chlorthalidone component may reduce the renal clearance of lithium leading to increased serum concentrations. Dose adjustments of lithium may therefore be necessary.

Other medicines for which increased toxicity has been reported when given concomitantly with chlorthalidone as contained in TENCHLOR include allopurinol and tetracyclines.

Diabetic medicines

Blood-glucose concentrations should be monitored in patients taking anti-diabetic medicines, since requirements may change. Chlorthalidone as contained in TENCHLOR may alter the requirements for hypoglycaemic medicines in diabetic patients. Concomitant use with insulin and oral antidiabetic medicines may lead to the intensification of the blood sugar lowering effects of these medicines.

Cholestipol and colestyramine

Gastrointestinal absorption has been reported to be reduced by cholestipol and colestyramine. The milk-alkali syndrome is characterised by hypercalcaemia, metabolic alkalosis, and renal failure. Patients taking chlorthalidone as contained in TENCHLOR may be at increased risk of developing the milk-alkali syndrome, because of their reduced ability to excrete excess calcium. Hypercalcaemia may also occur in patients taking chlorthalidone with medicines that

increase calcium levels, such as vitamin D.

Diagnostic tests

Chlorthalidone as contained in TENCHLOR may interfere with a number of diagnostic tests, including tests for parathyroid function; serum concentrations of protein-bound iodine may increase without signs of thyroid disturbance. Reported to diminish the response to pressor amines, such as noradrenaline.

Due to the combination medicine:

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

Concomitant use of baclofen may increase the antihypertensive effect making dose adjustments necessary when using TENCHLOR.

4.6 Fertility, pregnancy and lactation

TENCHLOR is contraindicated in pregnancy and lactation (see section 4.3).

Pregnancy

Administration to pregnant women shortly before giving birth, or during labour has resulted in bradycardia and other adverse effects such as hypoglycaemia and hypotension in the neonate and it may result in the newborn infants being born hypotonic, collapsed and hypoglycaemic.

Chlorthalidone as contained in TENCHLOR crosses the placenta and there have been reports of neonatal jaundice, thrombocytopenia, and electrolyte imbalances following maternal treatment. Reductions in maternal blood volume could also adversely affect placental perfusion.

Breastfeeding

Atenolol as contained in TENCHLOR is excreted into breast milk. Consult your medical practitioner. Chlorthalidone as contained in TENCHLOR is excreted and distributed in the breast milk. Treatment with chlorthalidone as contained in TENCHLOR can inhibit lactation.

Fertility

No data on fertility available.

4.7 Effects on ability to drive and use machines

TENCHLOR has minor influence on the ability to drive and use machines.

Since adverse reactions such as dizziness, drowsiness and visual disturbances have been reported in patients receiving TENCHLOR, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that TENCHLOR does not adversely affect their ability to do so (see section 4.4 and 4.8).

4.8 Undesirable effects

a) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Blood and the lymphatic system disorders		Purpura, thrombocytopenia, leucopenia (related to chlorthalidone) granulocytopenia, aplastic and haemolytic anaemia, agranulocytosis	Blood dyscrasias, transient eosinophilia
Immune system disorders			Hypersensitivity reactions, photosensitivity reactions
Metabolism and nutrition disorders		Fluid retention, weight gain	Hyperglycaemia, glycosuria hypochloraemic alkalosis, hyponatraemia, gout, hypokalaemia, hypercalcaemia, hypomagnesaemia, increase dconcentration of low-density and very low-density lipoprotein cholesterol, as well as of

			triglycerides, electrolyte imbalance, anorexia
Psychiatric disorders		Mood changes, nightmares, confusion, psychoses,hallucinations, sleep disturbances of the type noted with other beta blockers	
Nervous system disorders		Dizziness, headache, paraesthesia	Depression, peripheral neuropath, myopathies
Eye disorders		Dry eyes, visual disturbances	Decreased tear production, blurred vision, and soreness are among the ocular symptoms, yellow vision, choroidal effusion
Ear and labyrinth disorders			Loss of hearing
Cardiac disorders	Bradycardia	Heart failure, deterioration, precipitation of heart block	
Vascular disorders	Cold extremities	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		Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints, acute interstitial pneumonitis, acute pulmonary oedema,	Pneumonitis, pleurisy, pulmonary fibrosis
Gastrointestinal disorders	Gastrointestinal disturbances (including nausea related to chlorthalidone)	Dry mouth	Constipation vomiting, diarrhoea, abdominal cramping, pancreatitis stomatitis, sclerosing peritonitis, retroperitoneal fibrosis, gastric irritation
Hepato-biliary disorders		Hepatic toxicity including intrahepatic cholestasis, pancreatitis (related to chlorthalidone),	Cholestatic jaundice
Skin and subcutaneous tissue disorders		Alopecia (reversible), psoriasiform skin reaction, exacerbation of psoriasis, skin rashes	Angioedema and urticaria, pruritus
Musculoskeletal and connective tissue disorders			Lupus-like syndrome, muscle cramps
Reproductive system and breast disorders		Male impotence	

General disorders and administrative site conditions	Fatigue		Weakness, fever
Investigations		Elevations of transaminase levels, increase in ANA (Antinuclear Antibodies)	

b) Description of selected adverse reactions

Atenolol

Cardiac disorders

Cardiovascular effects may be precipipated in patients with underlying cardiac disorders.

Vascular disorder

Reduced peripheral circulation can produce coldness of the extremities and may exacerbate peripheral vascular disease such as Raynaud's syndrome. Abrupt withdrawal of beta-blockers may exacerbate angina and may lead to sudden death.

Respiratory, thoracic and mediastinal disorders

Bronchospasm may occur, particularly in susceptible individuals..

Chlorthalidone

Eye disorders

Cases of choroidal effusion with visual field defect have been reported after the use of thiazide and thiazide-like diuretics.

Investigations

Chlorthalidone may cause a number of metabolic disturbances at high doses and may cause hyperuricaemia and precipitate attacks of gout in some patients.

Chlorthalidone may provoke hyperglycaemia and glycosuria in diabetic and other susceptible patients.

Administration of chlorthalidone may be associated with electrolyte imbalances including hypochloraemic alkalosis, hyponatraemia, and hypokalaemia.

They may cause hyperglycaemia and aggravate or unmask diabetes mellitus. Chlorthalidone may increase the concentration of low-density and very low-density lipoprotein cholesterol, as well as of triglycerides. Acute interstitial pneumonitis and acute pulmonary oedema are less frequent but potentially dangerous complications of chlorthalidone therapy and may be due to a hypersensitivity reaction. Hypokalaemia in patients treated with chlorthalidone may be avoided or treated by concurrent administration of potassium or a potassium-sparing diuretic.

The urinary excretion of calcium is reduced, sometimes resulting in mild hypercalcaemia. Hypomagnesaemia has also occurred. There is some evidence to suggest that electrolyte imbalances during long-term treatment with chlorthalidone may be associated with an increased incidence of cardiac dysrhythmias. Signs of electrolyte imbalance include dry mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pain and cramps, seizures, oliguria, hypotension, and gastrointestinal disturbances.

Immune system disorders

Hypersensitivity reactions include skin rashes, fever, pulmonary oedema, and pneumonitis. Cholestatic jaundice, pancreatitis, and blood dyscrasias including thrombocytopenia and, less frequently granulocytopenia, leucopenia, and aplastic and haemolytic anaemia have been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Symptoms

Overdosage with atenolol may produce bradycardia and severe hypotension. Bronchospasm and heart failure may be produced in certain individuals. Coma and convulsions have been reported following beta-blocker (atenolol) overdosage.

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

Treatment

General treatment should include close supervision, treatment in an intensive care ward, activated charcoal and a laxative to prevent absorption of any medicine still present in the gastrointestinal tract, the use of plasma or plasma substitutes to treat hypotension and shock. The possible use of haemodialysis or haemoperfusion may be considered.
Excessive bradycardia may be countered with atropine 1 to 2 mg intravenously and/or a cardiac pacemaker. If necessary, this may be followed by a bolus dose of glucagon 10 mg intravenously. If required, this may be repeated or followed by an intravenous infusion of glucagon 1 to 10 mg/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 effects could 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.

Excessive diuresis should be countered by maintaining normal fluid and electrolyte balance.

5 PHARMACOLOGICAL PROPERTIES

5.1 Phamacodynamic properties

Class and category: A 7.1.3 Other hypotensives

Pharmacotherapeutic group: Vascular medicines

ATC code: C07BB03

Mechanism of action

Atenolol is a cardio-selective ß1-adrenergic receptor blocking medicine with insignificant partial agonist activity and weak membrane-stabilising properties. As it is highly hydrophilic it does not readily cross the blood brain barrier.

Chlorthalidone has the same actions as the thiazide diuretics although not chemically the same. Chlorthalidone acts directly on the kidney to increase the excretion of sodium chloride and an accompanying volume of water, it also increases the excretion of potassium. The major hypotensive effect during chronic administration appears to be due to vasodilatation, rather than to loss of water per se. However, the effect on peripheral vascular resistance may be secondary to diuretic-induced changes in sodium balance.

TENCHLOR has a narrow dose range and early patient response allows assessment of the effect within one or two weeks, in those patients who respond.

5.2 Pharmacokinetic properties

Absorption

Co-administration of chlorthalidone and atenolol has little effect on the pharmacokinetics of either. Absorption of atenolol following oral dosing is consistent but incomplete (approximately 40 to 50 %) with peak plasma concentrations occurring 2 to 4 hours after dosing. Approximately 60 % of an oral dose of chlorthalidone is absorbed from the gastrointestinal tract.

Distribution

Atenolol is only poorly bound to plasma proteins. Chlorthalidone is 75 % plasma protein bound. The tmax for atenolol is 3 hours and the tmax for chlorthalidone is 12 hours.

Biotransformation

Metabolism of atenolol occurs to only a very minor extent.

Elimination

Atenolol and chlorthalidone are excreted predominantly via the kidney. The elimination half-life of atenolol is 6 to 9 hours and that for chlorthalidone is approximately 50 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, povidone, purified talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the container tightly closed.

Keep in original packaging until required for use.

6.5 Nature and contents of container

TENCHLOR and TENCHLOR HS:

28 or 30 film-coated tablets are packed in a round, white, high density polyethylene bottle sealed with a round, white opaque polypropylene cap with induction sealing wad, together with rayon or a foam insert, two silica gel bags or desiccant disc, and a leaflet.

28 or 30 film-coated tablets are packed in a cylindrical, white, polypropylene container sealed with a round, white, low density polyethylene tamper evident cap, together with rayon or a foam insert, two silica gel bags or desiccant disc, and a leaflet.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

TENCHLOR: W/7.1.3/53

TENCHLOR HS: Z/7.1.3/96

9. DATE OF FIRST AUTHORISATION

TENCHLOR: 11 April 1989

TENCHLOR HS: 04 September 1991

10. DATE OF REVISION OF TEXT

21 May 2023

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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