Approved Professional Information for Medicines for Human Use:

HYDROCHLOROTHIAZIDE 25 ASCENDIS

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

HYDROCHLOROTHIAZIDE 25 ASCENDIS TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each HYDROCHLOROTHIAZIDE 25 ASCENDIS tablet contains 25 mg hydrochlorothiazide.

Contains sugar: lactose monohydrate 80 mg per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

HYDROCHLOROTHIAZIDE 25 ASCENDIS are white to off white round, biplanar tablets with a facette and a cross score notch.

Diameter: 8,0 ± 0,2 mm. Height 2,6 ± 0,2 mm

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oedema

- Due to sodium and water retention.
- associated with congestive cardiac failure, hepatic cirrhosis, nephrotic syndrome.

- Paradoxically, HYDROCHLOROTHIAZIDE 25 ASCENDIS appears to have an antidiuretic effect on patients with diabetes insipidus and may be of value in the management of the disease.

Hypertension

- Hydrochlorothiazide may be used alone or in combination with other antihypertensive agents.

4.2 Posology and method of administration

Posology

Therapy should be initiated at the lowest dose required to achieve the desired effect. Treatment should be individualised.

Adults

Oedema:

Usual dose is 25 mg to 50 mg per day. When adequate control of oedema has been achieved, the patient may be maintained on one tablet per day. In order to minimise excessive response and undesirable electrolyte imbalance, the dose may be administered on alternate days or on three to five days each week.

An initial dose of up to 200 mg may be necessary in some patients, but larger doses have no additional effect.

The maximum recommended daily dose is 100 mg.

Hypertension:

Usual dose is 12,5 mg to 25 mg daily as a single dose. The initial dosage should be 12,5 mg, whether hydrochlorothiazide is used as a single preparation or in combination. Dosage should be adjusted until the desired blood pressure is obtained and maintained. The maximum recommended daily dose is 100 mg.

It may be necessary to decrease the dose of concomitantly administered antihypertensives, in order to avoid an excessive decrease in blood pressure.

The dosage should not be higher than necessary to achieve the desired effect. Prolonged treatment may result in potassium ion loss. Potassium supplements may be necessary.

Paediatric population

2,5 mg per kg body mass daily in 2 divided doses.

Method of administration

For oral administration.

4.3 Contraindications

- Hypersensitivity to the hydrochlorothiazide or any other sulphonamide-derived medicines or to any of the excipients listed in section 6.1.
- Patients with anuria or severe renal (creatinine clearance < 30 mL/min) impairment.
- Patients with severe hepatic impairment.
- Patients with Addison's disease.
- Patients with pre-existing hypercalcaemia.
- The second and third trimesters of pregnancy and during lactation (see section 4.6).
- Patients with a history of previous and/or current basal cell carcinomas and/or squamous cell carcinomas of the skin and lip.

4.4 Special warnings and precautions for use

Hepatic disease

Use with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations in fluid or electrolyte balance may precipitate hepatic coma. Patients with hepatic cirrhosis are particularly at risk from hypokalaemia.

Metabolic

Glucose tolerance is impaired by hydrochlorothiazide, therefore the dosage of antidiabetic agents including insulin may have to be adjusted.

Hydrochlorothiazide may cause hyperglycaemia and aggravate or unmask diabetes mellitus.

Patients with cirrhosis of the liver are particularly at risk from hypokalaemia.

Electrolyte imbalance

The patient should be carefully observed for signs and symptoms of electrolyte and fluid imbalance, which include thirst, dryness of mouth, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, oliguria, hypotension, tachycardia and gastrointestinal disturbances such as nausea and vomiting.

It is particularly important to make urine and serum electrolyte determinations when the patient is vomiting excessively or receiving parenteral fluids. Careful check should be kept for signs of hyponatremia, hypochloraemic alkalosis, hypokalaemia and hypomagnesemia.

Hypokalaemia may develop with hydrochlorothiazide, especially following brisk diuresis and prolonged therapy, or hepatic cirrhosis and with concomitant ACTH or steroid administration.

Hypokalaemia can sensitize or exaggerate the response of the heart to the toxic effects of digitalis.

Diuretic induced hyponatremia may occur.

Elderly patients are particularly susceptible to electrolyte imbalance.

Hyperuricaemia

Hyperuricemia and / or gout may be precipitated in patients receiving hydrochlorothiazide.

Hypercalcaemia

Since the urinary excretion of calcium is decreased, elevation of serum calcium, in the absence of disorders of calcium metabolism may occur. Hydrochlorothiazide therapy should be withdrawn before carrying out parathyroid function tests.

Cholesterol and triglyceride levels

Increases in cholesterol and triglyceride levels may be associated with HYDROCHLOROTHIAZIDE 25 ASCENDIS therapy.

Hypomagnesaemia

Thiazides, including HYDROCHLOROTHIAZIDE 25 ASCENDIS, have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesaemia.

Impaired Renal Function and / or Azotaemia

HYDROCHLOROTHIAZIDE 25 ASCENDIS should be given with caution in renal function impairment since they can further reduce renal function (see section 4.3).

Hydrochlorothiazide, as in HYDROCHLOROTHIAZIDE 25 ASCENDIS is ineffective once creatinine clearance falls below 30 mL/min. Azotaemia may be precipitated or aggravated by hydrochlorothiazide.

If renal function is impaired, cumulative effects of the medicine may be observed.

If increasing azotaemia and oligouria occur, during treatment of severe progressive renal disease, the diuretic should be discontinued.

Hypokalaemia

Hypokalaemia may develop, especially with brisk diuresis when severe cirrhosis is present, in patients receiving concomitant therapy with corticosteroids or adrenocorticotropic hormone (ACTH) also known as corticotropin, or after prolonged therapy. Interference with adequate oral electrolyte intake will also contribute to hypokalaemia. Hypokalaemia may cause cardiac dysrhythmia and may also sensitise or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Hypokalaemia may be avoided or treated by use of potassium sparing diuretics or potassium supplements such as foods with a high potassium content.

Chloride deficit

Although any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease), chloride replacement may be required in the treatment of metabolic alkalosis.

Hyponatraemia

Dilutional hyponatraemia may occur in oedematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt, except in rare instances when the hyponatremia is life threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Systemic lupus erythematosus (SLE)

There is a possibility that HYDROCHLOROTHIAZIDE 25 ASCENDIS may exacerbate or activate systemic lupus erythematosus in susceptible patients.

Antihypertensive medicines

HYDROCHLOROTHIAZIDE 25 ASCENDIS may add to or potentiate the action of other antihypertensive medicines (see section 4.5).

Lithium

Lithium should generally not be given with diuretics (see section 4.5).

Eye disorders

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

Sulphonamide or sulphonamide 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 HYDROCHOLOROTHIAZIDE 25

ASCENDIS 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 sulphonamide or penicillin allergy.

Post-sympathectomy

The antihypertensive effects of HYDROCHOLOROTHIAZIDE 25 ASCENDIS may be enhanced in the post-sympathectomy patient.

Anti-doping test

HYDROCHOLOROTHIAZIDE 25 ASCENDIS could produce a positive analytical result in an anti-doping test.

Hypersensitivity reactions

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

Non-melanoma skin cancer

An increased risk of non-melanoma skin cancer (NSCLC) [basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)] has been observed with exposure to increasing cumulative doses of hydrochlorothiazide (HCTZ) in two epidemiological studies. Photosensitizing actions of HCTZ could act as a possible mechanism for NMSC.

Patients taking HYDROCHLOROTHIAZIDE 25 ASCENDIS should be informed of the risk of NMSC and advised to regularly check their skin for new lesions and promptly report any suspicious skin lesions. Possible preventative measures such as limited exposure to sunlight and UV rays and, in the case of exposure, adequate protection should be advised to the patients to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. HYDROCHLOROTHIAZIDE 25 ASCENDIS should not be used by patients who have had previous and/or current basal cell carcinomas and/or squamous cell carcinomas of the skin or lip (see section 4.3).

Excipient lactose

This medicine contains lactose:

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

Antidiabetic medications (oral agents or insulin)

Thiazide diuretics, as in HYDROCHLOROTHIAZIDE 25 ASCENDIS, reduce insulin sensitivity by increasing glucose intolerance and hyperglycaemia. For this reason, hydrochlorothiazide has interactions with all antidiabetics, whether oral or insulin, with a corresponding loss of diabetes control. Therefore, diabetic patients initiating treatment with HYDROCHLOROTHIAZIDE 25 ASCENDIS should carefully monitor their blood glucose levels and adjust their doses of antidiabetics appropriately.

Baclofen

Increased antihypertensive effect. Blood pressure and renal function should be monitored and the dosage of the antihypertensive should be adapted.

ACE inhibitors

Possible potentiation of toxicity with the presence of hypokalaemia.

Cholestyramine and colestipol resins

Absorption of hydrochlorothiazide is decreased or delayed in the presence of ion exchange resins. Single doses of cholestyramine or colestipol bind hydrochlorothiazide, as in HYDROCHLOROTHIAZIDE 25 ASCENDIS, and reduce its gastrointestinal absorption by up to 85 % and 43 %, respectively. It is recommended to administer thiazides at least 4 hours before

cholestyramine. The same goes for colestipol, although to a lesser degree, so it is recommended to administer thiazides at least 2 hours before.

Amphotericin B (parenteral), carbenoxolone, corticosteroids, corticotropin (ACTH) or stimulant laxatives

HYDROCHLOROTHIAZIDE 25 ASCENDIS may intensify electrolyte disturbance, especially hypokalaemia. Concomitant use of hydrochlorothiazide with amiloride, spironolactone or triamterene may reduce the risk of hypokalaemia due to its potassium-sparing effects. The use of these medicines may be an alternative to potassium supplements that are recommended for patients treated with diuretics. The risk of hydrochlorothiazide-induced hypokalaemia is higher if administered concomitantly with other medicines that also reduce plasma potassium levels such as corticosteroids (corticotropin, amphotericin B). In these cases it is recommended to monitor potassium levels and heart function, adding potassium supplements if necessary. Likewise, potassium levels should be normalized in case of administration of dofetilide, whose clearance is reduced by hydrochlorothiazide, with the corresponding risk of torsades de pointes.

Pressor amines (e.g., adrenaline, epinephrine)

HYDROCHLOROTHIAZIDE 25 ASCENDIS may decrease the response to pressor amines (norepinephrine/noradrenaline), but not enough to prevent their use.

Non-depolarizing muscle relaxants (e.g., turbocurarine): HYDROCHLOROTHIAZIDE 25 ASCENDIS may potentiate the action of curare derivatives, such as turbocurarine.

Lithium

Concomitant administration of HYDROCHLOROTHIAZIDE 25 ASCENDIS and lithium is not generally recommended since HYDROCHLOROTHIAZIDE 25 ASCENDIS may reduce the renal clearance of lithium and may lead to toxic blood concentrations of lithium (see section 4.4).

Nonsteroidal anti-inflammatory drugs (indomethacin)

Inhibition of renal prostaglandin synthesis produced by nonsteroidal anti-inflammatory drugs may reduce the diuretic, natriuretic, and antihypertensive effects of hydrochlorothiazide. It may also increase the risk of kidney failure by reducing renal blood flow. Careful monitoring of these patients is recommended to check for any change in the effectiveness of diuretic treatment or any symptoms of renal impairment and, if necessary, to hydrate the patient.

Calcium salts

An increase in serum calcium levels may occur due to a decrease in urinary excretion, when administered concomitantly with thiazide diuretics as in HYDROCHLOROTHIAZIDE 25 ASCENDIS, which may cause hypercalcemia.

Cardiac glycosides

Increases the possibility of digitalis toxicity (digoxin), associated with thiazide-induced hypokalaemia. It is recommended to monitor electrolytes and correct any imbalances when initiating treatment with digoxin or arsenic trioxide.

Medicines associated with Torsades de pointes (sultopride)

Due to the risk of hypokalaemia, caution should be exercised when administering hydrochlorothiazide as in HYDROCHLOROTHIAZIDE 25 ASCENDIS with medicines associated with torsades de pointes, e.g., some antiarrhythmics (e.g., quinidine, hydroquinidine, disopyridine, amiodarone, sotalol, dofetilide, ibutilide), some antipsychotics (e.g. thioridazine, clopromazine, levomepromazine, sulpiride, haloperidol) and other medicinal products known to induce Torsades of Pointes (e.g.: Ketanserin, mizolastine, vincamine, cisapride, erythromycin IV).

Carbamazepine

Concomitant use of carbamazepine and hydrochlorothiazide as in HYDROCHLOROTHIAZIDE 25 ASCENDIS has been associated with the risk of symptomatic hyponatremia. The electrolyte level should be monitored during this concomitant administration. If possible, another class of diuretic should be given.

Ciclosporin

Concomitant treatment with ciclosporin may increase the risk of hyperuricemia and gouty complications.

Tetracyclines

Concomitant administration of tetracyclines and thiazide diuretics increases the risk of tetracycline induced urea increase. This interaction probably does not apply to doxycycline.

Anticholinergic agents (e.g. atropine, biperidine)

The bioavailability of thiazide diuretics as in HYDROCHLOROTHIAZIDE 25 ASCENDIS may be increased with anticholinergic medicines, due to a decrease in gastrointestinal motility and stomach emptying rate.

Medicines used for the treatment of gout (probenecid, sulfinpyrazone, and allopurinol)

Dosage adjustment of uricosuric medication may be necessary as hydrochlorothiazide as in HYDROCHLOROTHIAZIDE 25 ASCENDIS may raise the serum uric acid level. It may be necessary to increase the dose of probenecid or sulfinpyrazone. Concomitant administration of HYDROCHLOROTHIAZIDE 25 ASCENDIS, may increase the incidence of allopurinol-hypersensitivity reactions.

Beta-blockers and diazoxide

Concomitant use of hydrochlorothiazide as in HYDROCHLOROTHIAZIDE 25 ASCENDIS, with betablockers may increase the risk of hyperglycaemia. Thiazide diuretics, including hydrochlorothiazide, may increase the hyperglycaemic effect of diazoxide.

Methyldopa

Isolated cases of haemolytic anaemia have been reported in patients receiving concomitant treatment with hydrochlorothiazide as in HYDROCHLOROTHIAZIDE 25 ASCENDIS and methyldopa.

Amantadine

Thiazides, including HYDROCHLOROTHIAZIDE 25 ASCENDIS, may increase the risk of adverse effects due to amantadine by decreasing its tubular secretion.

Cytotoxic medicines (e.g. cyclophosphamide, methotrexate)

Thiazides, including HYDROCHLOROTHIAZIDE 25 ASCENDIS, may reduce renal excretion of cytotoxic medicinal products and potentiate their myelosuppressive effects.

Salicylates

In case of high doses of salicylates, HYDROCHLOROTHIAZIDE 25 ASCENDIS may potentiate the toxic effect of salicylates on the central nervous system. They can also cause hypokalaemia.

Antihypertensive medicines, alcohol, barbiturates and opioids

HYDROCHLOROTHIAZIDE 25 ASCENDIS may enhance the effect of other antihypertensive medicines, while postural hypotension associated with this therapy may be enhanced by concomitant ingestion of alcohol, barbiturates, or opioids. Diuretic therapy with HYDROCHLOROTHIAZIDE 25 ASCENDIS should be discontinued for 2 to 3 days prior to initiation of therapy with an ACE-inhibitor, to reduce the likelihood of first dose hypotension.

Other interactions

Thiazide diuretics, including HYDROCHLOROTHIAZIDE 25 ASCENDIS may increase the photosensitizing effects of some medicines such as griseofulvin, phenothiazines, sulphonamides and sulfonylureas, tetracyclines, retinoids and medicines used in photodynamic therapy.

Laboratory tests

HYDROCHLOROTHIAZIDE 25 ASCENDIS may cause analytical interference in the diagnosis of the bentiromide test.

HYDROCHLOROTHIAZIDE 25 ASCENDIS may cause decrease concentrations of PBI (protein-bound iodine) levels without any signs of thyroid disorder.

Because of their effects on calcium metabolism, thiazides may interfere with parathyroid function tests.

Iodine contrast medium

In case of diuretic-induced dehydration, there is an increased risk of acute renal failure, especially with high doses of iodine products. Patients should be rehydrated prior to administration.

4.6 Fertility, pregnancy and lactation

The safety of HYDROCHLOROTHIAZIDE 25 ASCENDIS in pregnancy and lactation has not been established (see section 4.3).

Pregnancy

There is limited experience with HYDROCHLOROTHIAZIDE 25 ASCENDIS during pregnancy, especially during the first trimester. HYDROCHLOROTHIAZIDE 25 ASCENDIS crosses the placenta barrier and appears in cord blood. There have been reports of neonatal jaundice, icterus, thrombocytopenia and electrolyte imbalances

following maternal treatment. Reductions in maternal blood volume could also adversely affect placental perfusion.

HYDROCHLOROTHIAZIDE 25 ASCENDIS should not be used for gestational oedema, gestational hypertension or preeclampsia
due to the risk of decreased plasma volume and placental hypoperfusion, without a beneficial effect on the course of the disease.
HYDROCHLOROTHIAZIDE 25 ASCENDIS should not be used for essential hypertension in pregnant women.

Lactation

HYDROCHLOROTHIAZIDE 25 ASCENDIS is distributed into breastmilk and is not recommended for use in lactation. HYDROCHLOROTHIAZIDE 25 ASCENDIS in high doses causing intense diuresis can inhibit the milk production.

Fertility

No data are available.

4.7 Effects on ability to drive and use machines

HYDROCHLOROTHIAZIDE 25 ASCENDIS may cause dizziness, headache and dizziness, so the ability to drive and use machines may be impaired, mainly at the beginning of treatment, or when the dosage is modified and also in combination with alcohol intake, but these effects depend on individual susceptibility. If dizziness, headache, or dizziness are experienced, these activities should be avoided.

4.8 Undesirable effects

b) Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and postmarket spontaneous reports with hydrochlorothiazide.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations		Sialadenitis	
Neoplasm benign, malignant and unspecified (including cysts and polyps)			Non-melanoma skin cancer (basal cell carcinoma and squamous cell carcinoma)
Blood and lymphatic system disorders		Aplastic anaemia, haemolytic anaemia, leukopenia, purpura, thrombocytopenia, blood dyscrasias	Agranulocytosis, neutropenia, bone marrow depression

Immune system disorders		Hypersensitivity reactions	Anaphylactic reactions, purpura
Metabolism and nutrition disorders	Electrolyte imbalances, Hypochloraemic alkalosis, hyponatraemia (may occur in patients with severe heart failure who are very oedematous, particularly with large doses in conjunction with restricted salt in the diet), and hypokalaemia (intensifies the effect of digitalis on cardiac muscle and administration of digitalis or its glycosides may have to be temporarily suspended)	Metabolic disturbances especially at high doses, hyperglycaemia and carbohydrate intolerance in diabetic and other susceptible patients, asymptomatic hyperuricaemia and precipitate attacks of gout in some patients, hypomagnesaemia, anorexia hypokalaemia, electrolyte imbalance (hyponatraemia, hypochloraemia, metabolic alkalosis, hypercalcaemia and hypokalaemia), increased cholesterol and triglycerides.	
Psychiatric disorders	Restlessness	Agitation, depression, sleep disorders.	

Nervous system disorders	Lethargy, drowsiness, seizures	Loss of appetite, paraesthesia, dizziness, vertigo, headache, weakness, restlessness.	Light-headedness
Eye disorders		xhantopsia (yellow vision)	Transient blurred vision, choroidal effusion, acute myopia and secondary acute angle-closure glaucoma
Ear and labyrinth disorders		Vertigo	
Cardiac disorders		allergic myocarditis, vasculitis	Cardiac dysrhythmias
Vascular disorders		Orthostatic hypotension (aggravated by barbiturates, alcohol or narcotics)	Necrotising angiitis (vasculitis, cutaneous vasculitis)
Respiratory, thoracic and mediastinal disorders		Pneumonitis, pulmonary oedema.	Respiratory distress

Gastrointestinal disorders	Gastrointestinal disturbances, dry mouth	Gastric irritation, nausea, vomiting, constipation, diarrhoea, intestinal ulceration has occurred following the administration of tablets containing thiazides with an enteric-coated core of potassium chloride, pancreatitis, cramping	
Hepatobiliary disorders		Intrahepatic cholestatic jaundice.	
Skin and subcutaneous tissue disorders		Photosensitivity reactions, skin rash	Erythema multiforme including Stevens-Johnson Syndrome, exfoliative dermatitis including toxic epidermal necrolysis (TEN), alopecia, cutaneous lupus erythematosus-like

			reactions, reactivation of cutaneous lupus erythematosus, urticaria
Musculoskeletal and connective tissue disorders	Muscle pain and cramps	Muscle spasm	
Renal and urinary disorders	Oliguria	glycosuria, urinary excretion of calcium is reduced	Renal failure, renal dysfunction, interstitial nephritis
Reproductive system and breast disorders		Impotence	
General disorders and administration site conditions	Thirst, weakness		Fever

b) Description of selected adverse reactions:

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

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 professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Suspected adverse reactions can also be reported directly to the HCR via medsafety@austell.co.za

4.9 Overdose

Symptoms

HYDROCHLOROTHIAZIDE 25 ASCENDIS can produce acute renal failure either from overdosage, producing saline depletion and hypovolaemia or, occasionally, as a result of a hypersensitivity reaction.

The most frequent signs and symptoms observed are those caused by electrolyte depletion (hypokalaemia, hypochloraemia, hyponatraemia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalaemia may accentuate cardiac dysrhythmias.

Treatment

In massive overdosage, treatment should be symptomatic, supportive and directed at fluid and electrolyte replacement. In cases of recent ingestion emesis or gastric lavage should be carried out. Dehydration, electrolyte imbalance, hepatic coma and hypotension should be corrected by established procedures. If required, give oxygen or artificial respiration for respiratory impairment. The degree to which HYDROCHLOROTHIAZIDE 25 ASCENDIS is removed by haemodialysis has not been established.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 18.0 Diuretics

Pharmacotherapeutic group: Diuretics

ATC Code: C03AA03

Hydrochlorothiazide acts both as a diuretic and antihypertensive.

It exerts its action by interfering with the distal renal tubular mechanism of electrolyte reabsorption.

It increases the excretion of sodium and chloride, which is accompanied by some loss of potassium, magnesium and bicarbonate.

Urinary calcium excretion is decreased.

5.2 Pharmacokinetic properties

Absorption

Hydrochlorothiazide is absorbed from the gastrointestinal tract, distributed throughout the extracellular space and diffuses across the placenta.

Distribution

Hydrochlorothiazide is distributed throughout the extracellular space and diffuses across the placenta.

Biotransformation

Diuresis occurs in about two hours, reaches a maximum in about four hours, and lasts for about twelve hours. Tolerance does not develop, and therapeutic efficacy is maintained when it is administered over long periods, but patients may not respond if their glomerular filtration rate is markedly reduced.

Elimination

The route of elimination is via the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch

Microcrystalline cellulose

Sodium Starch Glycollate

Colloidal silicon dioxide

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

Store in tight, well closed containers at or below 25 °C.

Keep blisters in the carton until required for use.

Protect from moisture.

KEEP OUT OF THE REACH OF CHILDREN.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Shanur Healthcare (Pty) Ltd

Loch House Unit 003

3A Eton Road, Parktown

Johannesburg, 2193

South Africa

Tel: +27 87 405 9660

8. REGISTRATION NUMBER

32/18.1/0418

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28 May 2018

10. DATE OF REVISION OF THE TEXT

To be allocated by the Authority