1.3.1.1. PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

RIDAQ-12,5 tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of RIDAQ-12,5 contains 12,5 mg hydrochlorothiazide.

Contains sugar: Lactose monohydrate 62,6 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

RIDAQ-12,5 is a round, white tablet, flat with bevelled edges, bisected on one side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RIDAQ-12,5 is indicated for:

- mild to moderate hypertension, alone or in combination with other anti-hypertensives.

4.2 Posology and method of administration

Posology

Adults

If a single dose is indicated, RIDAQ-12,5 should preferably be taken in the morning in order to minimise the effect of increased frequency of urination during sleep. RIDAQ-12,5 should be taken with or after meals to minimise stomach upset.

Hypertension

For the treatment of mild to moderate hypertension

Take one tablet (12,5 mg) daily.

As an adjunct in the treatment of hypertension

Take one to two tablets (12,5 mg to 25 mg) daily in conjunction with an anti-hypertensive medicine.

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

No data are available.

Method of administration

For oral administration.

4.3 Contraindications

RIDAQ-12,5 is contraindicated in:

- Patients with hypersensitivity to hydrochlorothiazide, other sulphonamide-derived medicines or to any of the excipients in RIDAQ-12,5 (see 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.
- Patients with a history of previous and/or current basal cell carcinomas and/or squamous cell carcinomas of the skin and lip.
- The second and third trimesters of pregnancy and during lactation (see section 4.6).

4.4 Special warnings and precautions for use

Hepatobiliary disorders

RIDAQ-12,5 should be used with caution in patients with impaired hepatic function or progressive liver disease since minor alterations of fluid and electrolyte balance may precipitate hepatic coma and increases the risk of hepatic encephalopathy.

Patients with hepatic cirrhosis are particularly at risk of hypokalaemia.

Renal and urinary disorders

RIDAQ-12,5 should be given with caution in renal function impairment since it can further reduce renal function (see section 4.3).

In patients with renal disease, RIDAQ-12,5 may precipitate azotaemia and oliguria. Cumulative effects of the medicine may develop in patients with impaired renal function. RIDAQ-12,5 is ineffective at creatinine clearance values of 30 mL/min or below (i.e. moderate or severe renal insufficiency). If progressive renal impairment becomes evident, as indicated by rising non-protein nitrogen, careful reappraisal of therapy is necessary, with consideration given to discontinuing diuretic therapy.

Diabetes mellitus

RIDAQ-12,5 may cause hyperglycaemia and aggravate or unmask diabetes mellitus. Blood-glucose concentrations should be monitored in patients taking antidiabetic medicines, including insulin and oral hypoglycaemic medicines, since requirements may change.

Electrolyte imbalance

All patients should be carefully observed for signs of fluid and electrolyte imbalance namely, hyponatremia, hyperchloremic alkalosis, and hypokalaemia; serum and urine electrolyte determinations are particularly important especially in the presence of vomiting or during parenteral fluid therapy. Elderly patients are particularly susceptible to electrolyte imbalance.

Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, confusion, seizures, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be done at appropriate intervals.

Hypokalaemia

Hypokalaemia may develop, especially with brisk diuresis, 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 sensitize 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.

Hyponatremia

Dilutional hyponatremia 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.

Hyperuricaemia

Hyperuricaemia may occur, or acute gout may be precipitated in certain patients receiving RIDAQ-12,5.

Hypomagnesaemia

RIDAQ-12,5 have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesaemia.

Hypercalcaemia

RIDAQ-12,5 may decrease urinary calcium excretion. RIDAQ-12,5 may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcaemia may be evidence of hidden hyperparathyroidism. RIDAQ-12,5 should be discontinued before carrying out tests for parathyroid function.

Cholesterol and triglyceride levels

Increases in cholesterol and triglyceride levels may be associated with RIDAQ-12,5 therapy.

Systemic lupus erythematosus (SLE)

There is a possibility that RIDAQ-12,5 may exacerbate or activate systemic lupus erythematosus in susceptible patients.

Antihypertensive medicines

RIDAQ-12,5 may add to or potentiate the action of other antihypertensive medicines.

History of allergy or bronchial asthma

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

Lithium

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

Acute myopia and secondary angle-closure glaucoma

RIDAQ-12,5, a sulphonamide, can cause an idiosyncratic reaction, resulting in acute 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 RIDAQ-12,5 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.

Choroidal effusion

Sulfonamide or sulfonamide derivative medicines, such as hydrochlorothiazide, as in RIDAQ-12,5, 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 medicines 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.

Non-melanoma skin cancer

An increased risk of non-melanoma skin cancer (NMSC) (basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)) with increasing cumulative dose of hydrochlorothiazide (HCTZ), as in RIDAQ-12,5, exposure has been observed in two epidemiological studies. Photosensitising actions of RIDAQ-12,5 could act as a possible mechanism for NMSC.

Patients taking RIDAQ-12,5 should be informed of the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Possible preventive measures such as limited exposure to sunlight and UV rays and, in case of exposure, adequate protection should be advised to the patients to minimise the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. RIDAQ-12,5 should not be used by patients who have had previous and/or current basal cell carcinomas and/or squamous cell carcinomas of the skin and/or lip (see section 4.3).

Post-sympathectomy

The antihypertensive effects of the medicine may be enhanced in the post-sympathectomy patient.

Anti-doping test

RIDAQ-12,5 could produce a positive analytical result in an anti-doping test.

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

Amphotericin B (parenteral), carbenoxolone or stimulant laxatives: RIDAQ-12,5 may intensify electrolyte imbalance, particularly hypokalaemia.

Antidiabetic medicines (insulin and oral antidiabetics): Dosage adjustment of the antidiabetic medicines may be necessary.

Calcium salts: Increased serum calcium levels due to decreased excretion may occur when administered concurrently with RIDAQ-12,5.

Colestyramine resin and colestipol: The presence of anionic exchange resins may delay or decrease absorption of RIDAQ-12,5. Sulphonamide diuretics should be taken at least one hour before or four to six hours after these medicines.

Digitalis glycosides: RIDAQ-12,5 may enhance the toxicity of digitalis glycosides by depleting serum-potassium concentrations.

Nondepolarising skeletal muscle relaxants (e.g. tubocurarine): RIDAQ-12,5 may enhance the neuromuscular blocking action of competitive muscle relaxants, such as tubocurarine.

Antihypertensive medicines, alcohol, barbiturates and opioids: RIDAQ-12,5 may enhance or potentiate the effect of other antihypertensive medicines, while postural hypotension associated with this therapy may be enhanced by concomitant ingestion of alcohol, barbiturates, or opioids.

Corticosteroids, ACTH, corticotropin, beta$_2$-agonists: The potassium-depleting effect of RIDAQ-12,5 may be enhanced by corticosteroids, ACTH or corticotropin and beta$_2$-agonists such as salbutamol.

Pressor amines: RIDAQ-12,5 has been reported to diminish the response to pressor amines, such as noradrenaline, but the clinical significance of this effect is uncertain.

Lithium: Concomitant administration of RIDAQ-12,5 and lithium is not generally recommended since RIDAQ-12,5 may reduce the renal clearance of lithium and may lead to toxic blood concentrations of lithium (see section 4.4).

Non-steroidal anti-inflammatory drugs (NSAIDs): In some patients, the administration of NSAIDs can reduce the diuretic, natriuretic and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when RIDAQ-12,5 and NSAIDs are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

Medicines associated with Torsades de pointes: Due to the risk of hypokalaemia, caution should be used when RIDAQ-12,5 is co-administered with medicines associated with torsades de pointes, e.g. anti-dysrhythmics, antipsychotics and other medicines known to induce Torsades de pointes.

Laboratory tests: RIDAQ-12,5 should be discontinued before carrying out tests for parathyroid function (see section 4.3).
RIDAQ-12,5 may cause diagnostic interference of the bentiromide test. RIDAQ-12,5 may decrease serum Protein Bound Iodine (PBI) levels without signs of thyroid disturbance.

4.6. Fertility, pregnancy and lactation

The safety of RIDAQ-12,5 in pregnancy and lactation has not been established (see section 4.3).

Pregnancy

There is limited experience with RIDAQ-12,5 during pregnancy, especially during the first trimester. RIDAQ-12,5 crosses the placenta and there have been reports of neonatal jaundice, thrombocytopenia, icterus and electrolyte imbalances following maternal treatment and is not recommended for use in pregnancy. Reductions in maternal blood volume could also adversely affect placental perfusion.

RIDAQ-12,5 should not be used for gestational oedema, gestational hypertension or pre-eclampsia due to the risk of decreased plasma volume and placental hypoperfusion, without a beneficial effect on the course of the disease.

RIDAQ-12,5 should not be used for essential hypertension in pregnant women.

Breastfeeding

RIDAQ-12,5 is distributed into breast milk, and is not recommended for use in lactation. Due to the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue RIDAQ-12,5, considering the importance of the medicine to the mother. RIDAQ-12,5 in high doses causing intense diuresis can inhibit the milk production.

Fertility

There is no data available.

4.7 Effects on ability to drive and use machines

RIDAQ 12,5 mg has moderate influence on the ability to drive and use machines. Since adverse reactions such as somnolence, dizziness and blurred vision have been reported in patients receiving RIDAQ 12, 5 mg, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that RIDAQ 12,5 mg does not adversely affect their ability to do so (see section 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)
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 the lymphatic system disorders		Blood dyscrasias, thrombocytopenia, granulocytopenia, leukopenia, aplastic anaemia, haemolytic anaemia	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	Metabolic disturbances especially at high doses, hyperglycaemia in diabetic and other susceptible patients, hyperuricaemia and precipitate attacks of gout in some patients, hypomagnesaemia, anorexia	

	digitalis or its glycosides may have to be temporarily suspended)		
Psychiatric disorders	Restlessness	Depression, sleep disturbances	
Nervous system disorders	Lethargy, drowsiness, seizures	Headache, dizziness, paraesthesia	Light-headedness
Eye disorders		Yellow vision (xanthopsia)	Transient blurred vision, choroidal effusion
Ear and labyrinth disorders		Vertigo	
Cardiac disorders			Cardiac dysrhythmias
Vascular disorders		Postural hypotension (aggravated by barbiturates, alcohol or narcotics)	Necrotising angiitis (vasculitis, cutaneous vasculitis)
Respiratory, thoracic and mediastinal disorders		Pulmonary oedema, pneumonitis	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	
Hepato-biliary disorders		Cholestatic jaundice	
Skin and subcutaneous tissue disorders		Photosensitivity reactions, skin rashes	Erythema multiforme including Stevens-Johnson Syndrome, exfoliative dermatitis including toxic epidermal necrolysis, 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 administrative site conditions	Thirst, weakness		Fever
Investigations		Adverse changes in plasma lipids have been noted but their clinical significance is unclear.	Increases in cholesterol and triglycerides

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 providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Symptoms

RIDAQ-12,5 can produce acute renal failure either from overdosage, producing saline depletion and hypovolaemia or, occasionally, as a result of a hypersensitivity reaction.

The most common 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 is symptomatic and supportive. Recommended treatment for overdose includes immediate evacuation of the stomach (emesis or gastric lavage); supportive, symptomatic treatment; monitoring of serum electrolyte concentrations and renal function and immediate institution of appropriate treatment for hypokalaemia. Correct dehydration, electrolyte imbalance, hepatic coma and hypotension by established procedures. If required, give oxygen or artificial respiration for respiratory impairment. The degree to which RIDAQ 12,5 is removed by haemodialysis has not been established.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 18.1 Diuretics

Pharmacotherapeutic group: Medicines acting on reno- urinary and genital system

ATC code: C03AA03

Mechanism of action

Hydrochlorothiazide is a diuretic which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excretion of sodium, potassium and chloride ions, and consequently of water. It also slightly increases bicarbonate excretion without appreciable alteration of the acid-base balance or the pH of the urine. It has a lowering effect on the blood pressure and enhances the action of other hypotensive medicines such as guanethidine, methyldopa and rauwolfia alkaloids.

5.2 Pharmacokinetic properties

Absorption

Hydrochlorothiazide is absorbed from the gastrointestinal tract.

Distribution

Then 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

Lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose PH 101, polysorbate 80, purified talc, sodium starch glycolate (Type A).

6.2 List of incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C in a well-closed container.

Protect from light and moisture.

6.5 Nature and contents of container

Tablets are available in one of the following packaging:

- Metallised layflat bags

Silver metallised layflat “bank bag” sealed with a perforated tear line (tender purposes only). Filled patient ready packs are stored in an outer clear, low density polyethylene bag (60 µm) along with leaflets for distribution. Each metallised layflat bag will contain 28 tablets.

- HDPE bottle

The tablets are packed in a white 60 ml high density polyethylene (HDPE) bottle, together with a rayon insert and sealed with a sealing foil and a white 33 mm polypropylene cap. A leaflet is placed on top of the rayon insert prior to capping and a label is placed on the bottle.

Each bottle will contain 30 tablets.

- Securitainers

The tablets are packed in a white, polypropylene securitainer (49 mm x 100 mm), together with a white foam insert and sealed with a white, low-density polyethylene (LDPE), closure (49 mm) with a tamper evident seal. A leaflet is placed on top of the

foam insert prior to capping and a label is placed on the securitainer. Each securitainer will contain 500 tablets.

- Blisters

The tablets are packed in a PVC or PVC/ PVDC blister of 28 and 30 tablets. The blisters are packed in a cardboard carton.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

A39/18.1/0399

9. DATE OF FIRST AUTHORISATION

23 September 2005

10. DATE OF REVISION OF TEXT

04 March 2023

Die Afrikaanse Professionele Inligting is op versoek beskikbaar.

Mediese Blitslyn: 0800 118 088

ZA_RIDATAB12.5_2303_00