Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

HIZIDE 50 MG TABLETS

2. Qualitative and quantitative composition

Each tablet contains Hydrochlorothiazide USP 50 mg.
Excipient with known effect: Each tablet contains 35.40 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablet.
White to off white colour, round shaped flat tablets plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

Hydrochlorothiazide Tablets USP are indicated as adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, and corticosteroid and estrogen therapy.

Hydrochlorothiazide Tablets USP have also been found useful in edema due to various forms of renal dysfunction such as nephrotic syndrome, acute glomerulonephritis, and chronic renal failure.

Hydrochlorothiazide Tablets USP are indicated in the management of hypertension either as the sole therapeutic agent or to enhance the effectiveness of other antihypertensive drugs in the more severe forms of hypertension.

4.2 Posology and method of administration

Therapy should be individualized according to patient response. Use the smallest dosage necessary to achieve the required response.

Adults;

For Edema

The usual adult dosage is 25 to 100 mg daily as a single or divided dose. Many patients with edema respond to intermittent therapy, i.e., administration on alternate days or on three to five days each week. With an intermittent

schedule, excessive response and the resulting undesirable electrolyte imbalance are less likely to occur.

For Control of Hypertension

The usual initial dose in adults is 25 mg daily given as a single dose. The dose may be increased to 50 mg daily, given as a single or two divided doses. Doses above 50 mg are often associated with marked reductions in serum potassium (see also PRECAUTIONS). Patients usually do not require doses in excess of 50 mg of hydrochlorothiazide daily when used concomitantly with other antihypertensive agents.

Infants and Children

For Diuresis and For Control of Hypertension

The usual pediatric dosage is 0.5 to 1 mg per pound (1 to 2 mg/kg) per day in single or two divided doses, not to exceed 37.5 mg per day in infants up to 2 years of age or 100 mg per day in children 2 to 12 years of age. In infants less than 6 months of age, doses up to 1.5 mg per pound (3 mg/kg) per day in two divided doses may be required.

4.3 Contraindications

Anuria
Hypersensitivity to this product or to other sulfonamide-derived drugs.

4.4 Special warnings and precautions for use

WARNINGS

Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides 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.

Thiazides may add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Lithium generally should not be given with diuretics.

PRECAUTIONS

General

All patients receiving diuretic therapy should be observed for evidence of fluid or electrolyte imbalance: namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are

particularly important when the patient is vomiting excessively or receiving parenteral fluids. 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.

Hypokalemia may develop, especially with brisk diuresis, when severe cirrhosis is present or after prolonged therapy.

Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Hypokalemia may cause cardiac arrhythmia and may also sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Hypokalemia may be avoided or treated by use of potassium sparing diuretics or potassium supplements such as foods with a high potassium content.

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.

Dilutional hyponatremia may occur in edematous 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.

Hyperuricemia may occur or acute gout may be precipitated in certain patients receiving thiazides.

In diabetic patients' dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus, latent diabetes mellitus may become manifest during thiazide therapy.

The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. If progressive renal impairment becomes evident, consider withholding or discontinuing diuretic therapy. Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

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

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

Laboratory Tests

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

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interactions

When given concurrently the following drugs may interact with thiazide diuretics.

Alcohol, barbiturates, or narcotics

Potentiation of orthostatic hypotension may occur.

Antidiabetic drugs - (oral agents and insulin) Dosage adjustment of the antidiabetic drug may be required.

Other antihypertensive drugs

Additive effect or potentiation.

Cholestyramine and colestipol resins

Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively.

Corticosteroids, ACTH

Intensified electrolyte depletion, particularly hypokalemia.

Pressor amines (e.g., norepinephrine)

Possible decreased response to pressor amines but not sufficient to preclude their use.

Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine)

Possible increased responsiveness to the muscle relaxant.

Lithium

Generally, should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with hydrochlorothiazide.

Non-steroidal Anti-inflammatory Drugs

In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when hydrochlorothiazide and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

Drug/Laboratory Test Interactions

Thiazides should be discontinued before carrying out tests for parathyroid

function.

4.6 Pregnancy and Lactation

Pregnancy

Teratogenic Effects - Pregnancy Category B

Routine use of diuretics during normal pregnancy is inappropriate and exposes mother and fetus to unnecessary hazard.

There is no satisfactory evidence that they are useful in the treatment of toxemia during pregnancy.

Thiazides are indicated in pregnancy when edema is due to pathologic causes, just as they are in the absence of pregnancy (see PRECAUTIONS: Pregnancy).

Use of diuretics to manage dependent edema in pregnancy, resulting from restriction of venous return by the gravid uterus so as to lower intravascular volume is illogical and unnecessary as it can properly be treated through elevation of the lower extremities and use of support stockings.

Studies in which hydrochlorothiazide was orally administered to pregnant mice and rats during their respective periods of major organogenesis at doses up to 3000 and 1000 mg hydrochlorothiazide/kg, respectively, provided no evidence of harm to the fetus.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects

Thiazides cross the placental barrier and appear in cord blood. There is a risk of fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions that have occurred in adults.

Nursing Mothers

Thiazides are excreted in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue hydrochlorothiazide, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

However, when driving vehicles or operating machinery it must be borne in mind that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy, in particular during initiation of treatment or when the dose is increased**.**

4.8 Undesirable effects

The following adverse reactions have been reported and, within each category, are listed in order of decreasing severity.

Body as a Whole

Weakness

Cardiovascular

Hypotension including orthostatic hypotension (may be aggravated by alcohol, barbiturates, narcotics or antihypertensive drugs)

Digestive

Pancreatitis, jaundice (intrahepatic cholestatic jaundice), diarrhea, vomiting, sialadenitis, cramping, constipation, gastric irritation, nausea, anorexia

Hematologic

Aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia

Hypersensitivity

Anaphylactic reactions, necrotizing angiitis (vasculitis and cutaneous vasculitis), respiratory distress including pneumonitis and pulmonary edema, photosensitivity, fever, urticaria, rash, purpura

Metabolic

Electrolyte imbalance (see PRECAUTIONS), hyperglycemia, glycosuria, hyperuricemia

Musculoskeletal

Muscle Spasm

Nervous System/Psychiatric

Vertigo, paresthesias, dizziness, headache, restlessness

Renal

Renal failure, renal dysfunction, interstitial nephritis (see WARNINGS) skin erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis, alopecia

Urogenital

Impotence

Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

4.9 Overdose

The most common signs and symptoms observed are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias.

In the event of overdosage, symptomatic and supportive measures should be employed. Emesis should be induced or gastric lavage performed. 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 hydrochlorothiazide is removed by hemodialysis has not been established.

The oral LD50 of hydrochlorothiazide is greater than 10 g/kg in the mouse and rat.

5. Pharmacological properties

5.1 Pharmacodynamic properties

The mechanism of the antihypertensive effect of thiazides is unknown. Hydrochlorothiazide does not usually affect normal blood pressure.

Hydrochlorothiazide affects the distal renal tubular mechanism of electrolyte reabsorption. At maximal therapeutic dosage all thiazides are approximately equal in their diuretic efficacy.

Hydrochlorothiazide increases excretion of sodium and chloride in approximately equivalent amounts. Natriuresis may be accompanied by some loss of potassium and bicarbonate.

After oral use diuresis begins within 2 hours, peaks in about 4 hours and lasts about 6 to 12 hours.

5.2 Pharmacokinetic properties

Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. When plasma levels have been followed for at least 24 hours, the plasma half-life has been observed to vary between 5.6 and 14.8 hours. At least 61 percent of the oral dose is eliminated unchanged within 24 hours. Hydrochlorothiazide crosses the placental but not the blood-brain barrier and is excreted in breast milk.

5.3 Preclinical safety data

Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up

to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcinogenicity in male mice.

Hydrochlorothiazide was not genotoxic in vitro in the Ames mutagenicity assay of Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 and in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations, or in vivo in assays using mouse germinal cell chromosomes, Chinese hamster bone marrow chromosomes, and the Drosophila sex-linked recessive lethal trait gene. Positive test results were obtained only in the in vitro CHO Sister Chromatid Exchange (clastogenicity) and in the Mouse Lymphoma Cell (mutagenicity) assays, using concentrations of hydrochlorothiazide from 43 to 1300 µg/mL, and in the Aspergillus nidulans non-disjunction assay at an unspecified concentration.

Hydrochlorothiazide had no adverse effects on the fertility of mice and rats of either sex in studies wherein these species were exposed, via their diet, to doses of up to 100 and 4 mg/kg, respectively, prior to conception and throughout gestation.

6. Pharmaceutical Particulars

6.1 List of Excipients

Lactose Monohydrate BP,
Microcrystalline Cellulose 101 BP
Pregelatinized Starch BP
Magnesium Stearate BP

6.2 Incompatibilities

Not Applicable.

6.3 Shelf-Life

24 months.

6.4 Special Precautions for storage

Store in a dry place below 30°C

Protect from light

Keep all medicines out of reach of children.

6.5 Nature and Content of container

Hizide is packed is aluminium /PVC blister strips that are contained in unit cartons along with the patient information leaflet.

Pack size: 10 x 10's.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Dinlas Pharma (Africa) Limited

Mombasa Road Syokimau

P.O Box 22661-00505

Nairobi-Kenya

8. Marketing Authorization Number

CTD8943

9. Date of first authorization/renewal of the authorization

Date of first authorization: 17.02.2023

Renewal of authorization: 17.04.2023

10. Date of revision of the text

10/05/2025