1. Name of the medicinal Product

Hydrochlorothiazide Tablets USP 25 mg

1.1 Strength

25 mg/tablet

1.2 Pharmaceutical Form

Oral Tablets

2. Qualitative and Quantitative Composition

2.1 Qualitative declaration

Hydrochlorothiazide USP

2.2 Quantitative declaration

Excipients with known effect

Each film coated tablet contains 35 mg of Lactose (as Lactose Monohydrate)

For full list of Excipients, see section 6.1.

3. Pharmaceutical Form

Oral Tablets

White to off-white coloured, round shaped, flat, uncoated tablets, breakline on one side and plain on other side.

4. Clinical Particulars

4.1 Therapeutic Indications

Hydrochlorothiazide is indicated as adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, and corticosteroid and estrogen therapy. Hydrochlorothiazide has been also found useful in edema due to various forms of renal dysfunction such as nephrotic syndrome, acute glomerulonephritis, and chronic renal failure. Hydrochlorothiazide is indicated in the management of hypertension either as the so le therapeutic agent or to enhance the effectiveness of other antihypertensive drugs in the more severe forms of hypertension.

4.2 Posology

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 mg 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 3 to 5 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. 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 paediatric dosage is 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 3 mg/kg per day in two divided doses may be required

4.3 Method of Administration

Oral Route

4.4 Contraindications

Hypersensitivity to hydrochlorothiazide or to other sulfonamide-derived drugs.

Anuria

4.5 Special Warnings and Special Precautions for Use

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

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

Hypokalemia: 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 high potassium content.

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

Hypomagnesemia: Thiazides have been shown to increase the urinary excretion of magnesium.

*Hyperglycemia***:** 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.

Hypercalcemia: Thiazides may decrease urinary calcium excretion. Thiazides may cause intem1ittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism.

Renal impairment: 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.

Hepatic impairment: Use with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Pregnancy: There are 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.

Lactation: 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.

Caution for use: It contains lactose. Patients with galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine

4.6 Paediatric Population

For Diuresis and for Control of Hypertension: The usual paediatric dosage is 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 3 mg/kg per day in two divided doses may be required

4.7 Interaction with other medicinal products and other forms of interaction

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%, respectively.

Corticosteroids, ACTH: intensified electrolyte depletion, particularly hypokalemia.

Skeletal Muscle Relaxants, No depolarizing (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.

Non-Sterodial Anti-inflammatory Drugs: Non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic and antihypertensive effects of loop, potassium-sparing and thiazide diuretics.

4.8 Additional information on special populations

No specific Information

4.9 Paediatric Population

No specific Information

4.10 Pregnancy and Lactation

4.10.1 Pregnancy

There are 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.

4.10.2 Lactation

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.

4.11 Effects on ability to Drive and use Machines

None

4.12 Undesirable Effects

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

Digestive: Pancreatitis, jaundice (intrahepatic cholestatic jaundice), diarrhea, vomiting, 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, hyperglycemia, glycosuria, hyperuricemia.

Musculoskeletal: Muscle spasm.

Nervous System/Psychiatric: Vertigo, paresthesias, dizziness, headache, restlessness.

Renal: Renal failure, renal dysfunction, interstitial nephritis.

Skin: Erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidennal necrolysis, alopecia.

Special Senses: Transient blurred vision, xanthopsia.

Urogenital: Impotence.

4.13 Overdose

Symptoms: 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. Treatment: In the event of over dosage, symptomatic and supportive

measures should be employed. Emesis should be induced or gastric lavage perfom1ed. Correct dehydration, electrolyte imbalance, hepatic coma and hypotension by established procedures. If required, give oxygen or artificial respiration for resp iratory impairment. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

5. Pharmacological Properties

5.1 Pharmacodynamics 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

Not Applicable

6. Pharmaceutical Particulars

6.1 List of Excipients

Microcrystalline Cellulose (Plain)

Lactose (Lactose Monohydrate)

Maize Starch BP

Purified Water BP

Sodium Starch Glycolate (Type - A)

Colloidal Anhydrous Silica (Aerosil)

Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Store below 30°C. Protect from light.

6.5 Nature and Contents of Container

10 Tablets are packed in a Alu-PVC Blister Pack. Such 10 Alu-PVC Blisters are packed in a printed carton along with package insert.

6.6 Special precaution for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder and Manufacturing Site Addresses

7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Tal.-Kalol,
Dist.- Gandhinagar, Gujarat, India.
Telephone no.: +91-079-41078096
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Tal.-Kalol,
Dist.- Gandhinagar, Gujarat, India.

Telephone no.: +91-079-41078096

Email: hiren@lincolnpharma.com

Website: www.lincolnpharma.com

8. Marketing Authorization Number

It will be applicable after registration of this product.

9. Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

10. Date of Revision of the Text

September, 2023

11. Dosimetry (If Applicable)

Not Applicable

12. Instructions for preparation of radiopharmaceuticals

Not Applicable