SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NEO-URIZIDE / Hydroflumethiazide Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hydroflumethiazide BP 50.00 mg. Also contains lactose.
For excipients see section 6.1

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NEO-URIZIDE is a diuretic used to reduce oedema of cardiac, renal or hepatic origin; also other types of oedema including iatrogenic oedema. It is also used in pre-menstrual tension.

NEO-URIZIDE is useful in the treatment of hypertension either alone or with a hypotensive agent.

4.2 Posology and method of administration

Adults:

Oedema: 50 to 200 mg daily, depending upon the severity of the oedema, as a single dose in the morning. The daily dose should be given early enough to complete diuresis by bedtime.

Antihypertensive: 25 to 50 mg daily; when given as an adjunct to other antihypertensive agents the dose of the latter should be halved.

Maintenance: Doses of 25 to 50 mg on alternate days are usually adequate for maintenance therapy.

Children over 12 years: Daily dosage in children will be at the discretion of the physician; 1 mg per kg of bodyweight has been suggested as suitable for most cases.

Elderly: The adult dosage of NEO-URIZIDE may need to be reduced in the elderly, particularly when renal function is impaired because of the possibility of electrolyte imbalance.

Route of administration: Oral

4.3 Contraindications

Hypersensitivity, severe renal or hepatic failure, Addisons disease, hypercalcaemia, symptomatic hyperuricaemia, refractory hypokalaemia, hyponatraemia and concurrent lithium therapy.

4.4 Special warnings and precautions for use

NEO-URIZIDE may precipitate or aggravate diabetes and may impair control of diabetes in patients receiving sulphonylureas.

Supplementary potassium is strongly recommended in patients receiving digitalis who require prolonged diuretic treatment.

May cause hypokalaemia, which may be corrected with potassium or a potassium-sparing drug. Renal function should be monitored.

Increased risk of hypomagnesaemia in alcoholic cirrhosis.

May aggravate gout. Serum uric acid levels may be raised with or without gout in some patients.

Treat with caution in hepatic or renal impairment (avoid if severe).

May aggravate systemic lupus erythematosus.

Blood dyscrasias and pancreatitis have been reported.

Patients on long-term treatment and elderly patients need blood tests to monitor blood electrolyte levels and blood dyscrasias.

Expectant mothers who receive thiazide diuretics may be at increased risk from acute haemorrhagic pancreatitis; thrombocytopenia has been reported in newborn infants following antepartum use of thiazides.

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

Choroidal effusion, acute myopia and secondary angle-closure glaucoma: Sulfonamide or sulfonamide derivative drugs 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 drug initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss, the primary treatment is to discontinue drug 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.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent therapy with carbenoxolone may necessitate potassium supplements. Sensitivity to digitalis may increase and signs of overdosage appear.

Potassium supplements should not be given in renal insufficiency complicated by hyperkalaemia.

Antagonism of diuretic effect may occur when used concurrently with non-steroidal anti-inflammatory drugs, (indometacin, ketorolac), corticosteroids and oestrogens & combined oral contraceptives.

Enhanced hypotensive effect when given with adrenergic neurone blockers, general anaesthetics, ACE inhibitors, angiotensin II antagonists, anxiolytics and hypnotics, calcium-channel blockers, beta-blockers, MAOIs, nitrates, phenothiazines, several antihypertensive drugs, alprostadil, aldesleukin, levodopa, baclofen, moxisylyte, tizanidine and alpha-blockers such as prazosin.

Increased risk of nephrotoxicity with NSAIDs, and of nephrotoxicity and ototoxicity with cisplatin.

Increased risk of nephrotoxicity and possibly hypermagnesaemia are also reported when thiazides and related diuretics are given with ciclosporin.

Corticosteroids, acetazolamide, amphotericin, reboxetine, $beta_2$ sympathomimetics, theophylline, loop diuretics may exacerbate hypokalaemia.

Hypokalaemia caused by thiazides and related diuretics:

Increases cardiac toxicity with cardiac glycosides, disopyramide, flecainide, amiodarone and quinidine

Antagonises action of lidocaine and mexiletine

Increases risk of ventricular arrhythmias with sotalol, amisulpride, atomoxetine, sertindole and terfenadine. Avoid concomitant use with pimozide.

There is an increased risk of postural hypotension with alcohol and tricyclic antidepressants.

Antagonism of hypoglycaemic effect of antidiabetic agents.

There is an increased risk of hypersensitivity when thiazides and related diuretics are given with allopurinol especially in renal impairment.

Increased risk of hyponatraemia if given with carbamazepine, chlorpropamide and aminoglutethimide.

Increased risk of hypercalcaemia with calcium salts, toremifene and vitamin D.

Increased risk of lithium toxicity with lithium salts when given concurrently with thiazide diuretics.

Colestipol and colestyramine may reduce the absorption of thiazides and related diuretics.

4.6 Pregnancy and lactation

i) Diuretics are best avoided for the management of oedema of pregnancy or hypertension in pregnancy as their use may be associated with hypovolaemia, increased blood viscosity and reduced placental perfusion.

ii) There is inadequate evidence of safety in human pregnancy. Foetal bone marrow depression and thrombocytopaenia as well as foetal and neonatal jaundice have also been described.

iii) As diuretics pass into breast milk they should be avoided in mothers who wish to breast feed.

4.7 Effects on ability to drive and use machines

Not known

4.8 Undesirable effects

Impotence. Mild anorexia or indigestion may be avoided by taking dose after meals.

The following have also been reported as undesirable effects of thiazide diuretics: postural hypotension, hypokalaemia, hyponatraemia, hypomagnesaemia, hypercalcaemia, hypochloraemic alkalosis, gout, hyperuricaemia, hyperglycaemia, altered plasma lipid concentrations, skin rashes, photosensitivity, blood disorders (including neutropenia and thrombocytopenia), hypersensitivity reactions, pancreatitis, intrahepatic cholestasis, bone marrow depression.

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

Gastrointestinal disorders, not known (frequency cannot be estimated from the available data): diarrhoea

4.9 Overdose

Treatment should be symptomatic and directed at monitoring blood pressure, fluid and electrolyte balance. In the case of recent ingestion, gastric lavage should be performed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The principal site of action of Hydroflumethiazide is on the distal convoluted tubule distal to the thick segment of the end limb of the loop of Henle. Hydroflumethiazide inhibits the distal tubular re-absorption of sodium and chloride ions. Increased delivery of sodium to ion exchange sites in the collecting duct results in increased urinary loss of potassium and also of magnesium. Hydroflumethiazide also enhances the renal tubular re-absorption of calcium. The antihypertensive effect is mainly due to sodium loss.

5.2 Pharmacokinetic properties

Hydroflumethiazide is incompletely but rapidly absorbed after oral administration. Plasma concentration peaks between 1 and 4 hours. Significant pre-systemic metabolism has been reported. Plasma elimination half-life varies from 12.4 to 26.9 hours after single doses. Between 40% and 80% of the drug is excreted unchanged in the urine. The remainder is metabolised. Plasma protein binding is approximately 75%. Volume of distribution averages 6.4 l/kg in normal subjects.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch

Pre-gelatinised maize starch
Sodium starch glycollate
Magnesium stearate

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25ºC in a dry place in well closed containers.

6.5 Nature and contents of container

High density polystyrene with polythene lids and/or polypropylene containers with polypropylene or polyurethane lids and polyurethane/polythene inserts.

Packs of 100, 500 and 1000 tablets.

6.6 Special precautions for disposal

No special instructions

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 33414/0048

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04/09/2020