SCHEDULING STATUS: S3

PROPRIETARY NAME AND DOSAGE FORM:
ADCO DAPAMAX (tablet)

COMPOSITION:
Each tablet contains:
Indapamide 2,5 mg
Contains sugar:
Lactose monohydrate 55 mg

PHARMACOLOGICAL CLASSIFICATION:
A 7.1 Vasodilators, hypotensive medicines

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties
Indapamide, an indole derivative of chlorosulphonamide, has an antihypertensive action causing a drop in systolic, diastolic and mean blood pressure. This antihypertensive action is maximal at a dose of 2,5 mg per day and the diuretic effect is slight, usually without clinical manifestation. At higher doses, the diuretic effect becomes more prominent. The extra-renal antihypertensive action of 2,5 mg per day is demonstrated as a decrease in vascular hyperreactivity and a reduction in total peripheral and arteriolar resistance. The extra-renal mechanism of action has also been demonstrated by the maintenance of antihypertensive effect in functionally anephric patients. The extra-renal action is thought to be due to the inhibition of transmembrane ionic influx, essentially calcic, and the stimulation of synthesis of the vasodilatory hypotensive prostaglandin PGE_2.
Pharmacokinetic properties:
Indapamide is rapidly and completely absorbed after oral administration. Peak blood levels are reached after 1 to 2 hours. Indapamide is extensively metabolised and only 5 to 7 % is found unchanged in the urine. The elimination half-life is 14 to 18 hours. Indapamide is 79 % bound to plasma protein. The methyl-indoline portion of the molecule gives indapamide its lipophilic character, and indapamide's lipid solubility is 5 to 8 times that of the thiazides. It is as a result of this characteristic that indapamide localizes in smooth vascular muscle.

INDICATIONS:
ADCO DAPAMAX (indapamide) is indicated in the management of mild to moderate hypertension, and oedema associated with congestive heart failure.

CONTRAINDICATIONS:
Hypersensitivity to the active ingredient or other sulphonamide-type medications. Patients with severe renal or hepatic dysfunction, or patients with Addison's disease.
Patients with pre-existing hypercalcaemia.

WARNINGS AND SPECIAL PRECAUTIONS:

Urinary excretion of calcium may be reduced, sometimes resulting in mild hypercalcaemia. Use with caution in patients with impaired hepatic function or renal impairment. Treatment should be discontinued if increasing azotaemia and oliguria occur. Elderly patients are particularly susceptible to electrolyte imbalance. Systemic lupus erythematosus may be exacerbated or activated in susceptible patients.

ADCO DAPAMAX contains lactose monohydrate. Patients with rare hereditary disorders such as galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not use **ADCO DAPAMAX**. Lactose monohydrate may have an effect on the glycaemic control of patients with diabetes mellitus.

INTERACTIONS:

Thiazide diuretics may enhance the toxicity of digitalis glycosides by depleting serum-potassium concentrations. They may enhance the neuromuscular blocking action of competitive muscle relaxants, such as tubocurarine. The effects of antihypertensive agents may be enhanced, while postural hypotension may be enhanced by concomitant ingestion of alcohol, barbiturates, or opioids. The potassium-depleting effect of thiazide diuretics may be enhanced by corticosteroids, corticotropin, or carbenoxolone. They are reported to diminish the response to pressor amines, such as noradrenaline, but the clinical significance is uncertain. Concomitant administration with lithium is not generally recommended since the association may lead to toxic blood concentrations of lithium.

NSAIDs may interfere with the efficacy of indapamide, and may enhance the risk of renal insufficiency.

The co-administration of **ADCO DAPAMAX** with other thiazide type diuretics is not recommended.

Laboratory tests:

Serum potassium should be monitored in patients prone to hypokalaemia and uric acid should be monitored in patients with a history of gout.

PREGNANCY AND LACTATION:

Safety during pregnancy and lactation have not been established.

DOSAGE AND DIRECTIONS FOR USE:

Hypertension:

Adults: The dosage is one tablet daily, preferably to be taken in the morning with breakfast. In more severe cases, **ADCO DAPAMAX** can be combined with other categories of antihypertensive agents. Dose may be increased to 5 mg (2 tablets) after 4 weeks.

Oedema:

One tablet daily, increased to two tablets daily after 1 week if necessary.

Children: There is no experience of the use of **ADCO DAPAMAX** in children.

SIDE EFFECTS:

Blood and the lymphatic system disorders:
Blood dyscrasias including thrombocytopenia and, less frequently, granulocytopenia, leucopenia, and aplastic and hemolytic anaemia have been reported.

Immune system disorders:
Hypersensitivity reactions include skin rashes, pulmonary oedema, and pneumonitis.

Metabolism and nutrition disorders:
A number of metabolic disorders may occur. Hyperglycaemia and glycosuria may be provoked in diabetic and other susceptible patients. Thiazide diuretics may cause hyperuricaemia and precipitate attacks of gout in some patients. Associated electrolyte imbalances including hypochloraemic alkalosis, hyponatraemia and hypokalaemia can occur and potassium supplementation may be required. Patients with cirrhosis of the liver are particularly at risk from hypokalaemia. Hyponatraemia may occur in patients with severe congestive heart failure. Hypomagnesaemia has also occurred.
Signs of electrolyte imbalance include dry mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pain and cramps, seizures, oliguria, and gastrointestinal disturbances.
Other side effects include anorexia.

Nervous system disorders:
Headache, dizziness.

Eye disorders:
Photosensitivity reactions and yellow vision.

Vascular disorders:
Postural hypotension, paraesthesia.

Gastrointestinal disorders:
Gastric irritation, nausea, vomiting, constipation, diarrhoea, pancreatitis.

Hepato-biliary disorders:
Cholestatic jaundice.

Reproductive system and breast disorders:
Impotence.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Refer to **SIDE EFFECTS AND WARNINGS AND SPECIAL PRECAUTIONS**.

Treatment:
In massive overdosage, treatment should be symptomatic and directed at fluid and electrolyte replacement. In the case of recent ingestion gastric lavage should be carried out.
Further treatment is symptomatic and supportive.

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IDENTIFICATION:
White, film-coated, round, biconvex tablet.

PRESENTATION:
Blisters of 30 and 600 tablets.
Securitainers of 1400 tablets.

STORAGE INSTRUCTIONS:
Store in a cool, dry place at or below 25 ºC
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:
30/7.1/0092

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
Adcock Ingram Limited
1 New Road,
Erand Gardens,
Midrand,
1685
Private Bag X69
Bryanston 2021
www.adcock.com

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