Duride® Tablets

(Co-amilofruse)

(Product Specs.: B.P.)

ڈیورائیڈ ٹیبلیٹس

(کوایمیلوفروز)

DESCRIPTION:
Furosemide is a diuretic which is an anthranilic acid derivative. Chemically, it is 4-chloro-Nfurfuryl-5-sulfamoylanthranilic acid. Furosemide is a white to off-white odorless crystalline powder. It is practically insoluble in water, sparingly soluble in alcohol, freely soluble in dilute alkali solutions and insoluble in dilute acids. Its molecular formula is $C_{12}H_{11}ClN_2O_5S$ and its molecular weight is 330.74.

Amiloride HCl, an antikaliuretic-diuretic agent, is a pyrazine-carbonyl-guanidine that is unrelated chemically to other known antikaliuretic or diuretic agents. It is the salt of a moderately strong base (pKa 8.7). It is designated chemically as 3,5-diamino-6-chloro-N-(diaminomethylene) pyrazinecarboxamide monohydrochloride, dihydrate and has a molecular weight of 302.12. Its empirical formula is $C_6H_8ClN_7O \cdot HCl \cdot 2H_2O$

COMPOSITION:
Each tablet contains: Furosemide B.P. ...40mg
Amiloride Hydrochloride Dihydrate B.P. eq. to
Amiloride Hydrochloride ...5mg
(Product Specs.: B.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic Group: High-ceiling diuretics and potassium-sparing agents
ATC code: C03CA01-Furosemide, C03DB01-Amiloride.

Mechanism Of Action:
FUROSEMIDE:
Furosemide is a potent loop diuretic which acts primarily to inhibit electrolyte reabsorption in the thick ascending loop of Henle. Excretion of sodium, potassium and chloride ions is increased and water excretion enhanced.

AMILORIDE:
Amiloride is a mild diuretic which moderately increases the excretion of sodium and chloride and reduces potassium excretion, and appears to act mainly on the distal renal tubules. It does not appear to act by inhibition of aldosterone and does not inhibit carbonic anhydrase. Amiloride adds to the natriuretic but diminishes the kaliuretic effects of other diuretics.

A combination of Furosemide and Amiloride is a diuretic which reduces the potassium loss of furosemide alone while avoiding the possible gastro-intestinal disturbances of potassium supplements.

Pharmacokinetic Properties
Furosemide:
Approximately 65% of the dose is absorbed after oral administration. The plasma half-life is biphasic with a terminal elimination phase of about 1½ hours. Furosemide is up to 99% bound to plasma proteins, and is mainly excreted in the urine, largely unchanged, but also excreted in the bile, non-renal elimination being considerably increased in renal failure. Furosemide crosses the placental barrier and is excreted in the milk.

Amiloride:
Approximately 50% of the dose is absorbed after oral administration and peak serum concentrations are achieved by three to four hours. The serum half-life is estimated to be about 6 hours. Amiloride is not bound to plasma proteins. Amiloride is not metabolised and is excreted unchanged in the urine.

THERAPEUTIC INDICATIONS:
Duride is a potassium sparing diuretic which is indicated where a prompt diuresis is required. It is of particular value in conditions where potassium conservation is important: congestive cardiac failure, nephrosis, fluid retention due to corticosteroid or oestrogen therapy and ascites associated with cirrhosis.

DOSAGE AND ADMINISTRATION:
The starting dose is usually 5/40mg, subsequent dosage being adjusted to suit the needs of the patient.

Adults:
One to two tablets to be taken in the morning.

Children:
Not recommended for children under 18 years of age as safety and efficacy have not been established.

Elderly:
The dosage should be adjusted according to diuretic response. Serum electrolytes and urea should be carefully monitored.

CONTRAINDICATIONS:
Patients with hypovolaemia or dehydration (with or without accompanying hypotension). Patients with an impaired renal function and a creatinine clearance below 30ml/min per 1.73 m2 body surface area, anuria or renal failure with anuria not responding to furosemide, renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents or renal failure associated with hepatic coma, hyperkalaemia, severe hypokalaemia, severe hyponatraemia, concomitant potassium supplements or potassium sparing diuretics, precomatose states associated with cirrhosis,

Addison's disease and breast feeding women.

Duride is contraindicated in children and adolescents less than 18 years of age, as safety in this age group has not been established.

Hypersensitivity to furosemide, amiloride, sulphonamides or sulphonamide derivatives, or any of the excipients of the product.

WARNINGS AND PRECAUTIONS:
Duride should be discontinued before a glucose tolerance test.
Duride Tablets should be used with particular caution in elderly patients or those with potential obstruction of the urinary tract or disorders rendering electrolyte balance precarious.

Urinary output must be secured. Patients with partial obstruction of urinary outflow, for example patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention and require careful monitoring.

Where indicated, steps should be taken to correct hypotension or hypovolaemia before commencing therapy.

Particularly careful monitoring is necessary in:
- Patients with hypotension.
- Patients who are at risk from a pronounced fall in blood pressure.
- Patients where latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.
- Patients with gout.
- Patients with hepatic cirrhosis together with impaired renal function.
- Patients with hypoproteinaemia, e.g. associated with nephrotic syndrome (the effect of furosemide may be weakened and its ototoxicity potentiated). Cautious dose titration is required.
- Symptomatic hypotension leading to dizziness, fainting or loss of consciousness can occur in patients treated with furosemide, particularly in the elderly, patients on other medications which can cause hypotension and patients with other medical conditions that are risks for hypotension.

Caution should be observed in patients liable to electrolyte deficiency. Regular monitoring of serum sodium, potassium, creatinine and glucose is generally recommended during therapy; particularly close monitoring is required in patients at high risk of developing electrolyte imbalances or in case of significant additional fluid loss. Hypovolaemia or dehydration as well as any significant electrolyte and acid-base disturbances must be corrected. This may require temporary discontinuation of Duride.

Frequent checks of the serum potassium level are necessary in patients with impaired renal function and a creatinine clearance below 60ml/min per 1.73m^2 body surface area as well as in cases where Duride is taken in combination with certain other drugs which may lead to an increase in potassium levels.

In patients who are at high risk for radiocontrast nephropathy, furosemide is not recommended to be used for diuresis as part of the preventative measures against radiocontrast-induced nephropathy.

Duride contains sunset yellow
May cause allergic reactions.

Duride contains lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

DRUG INTERACTIONS:
The dosage of concurrently administered cardiac glycosides, diuretics, anti-hypertensive agents, or other drugs with blood-pressure-lowering potential may require adjustment as a more pronounced fall in blood pressure must be anticipated if given concomitantly with Duride.

A marked fall in blood pressure and deterioration in renal function may be seen when ACE inhibitors or angiotensin II receptor antagonists are added to furosemide therapy, or their dose level increased. The dose of Duride should be reduced for at least three days, or the drug stopped, before initiating the ACE inhibitor or angiotensin II receptor antagonist or increasing their dose.

When amiloride is taken in combination with potassium salts, with drugs which reduce potassium excretion, with nonsteroidal anti-inflammatory drugs or with ACE inhibitors, an increase in serum potassium concentration and hyperkalaemia may occur.

The toxic effects of nephrotoxic drugs may be increased by concomitant administration of potent diuretics such as furosemide.

Oral Duride and sucralfate must not be taken within 2 hours of each other because sucralfate decreases the absorption of furosemide from the intestine and so reduces its effect.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with Duride, resulting in increased lithium toxicity, including increased risk of cardiotoxic and neurotoxic effects of lithium. Therefore, it is recommended that lithium levels are carefully monitored and where necessary the lithium dosage is adjusted in patients receiving this combination.

Amiloride may cause raised blood digoxin levels. Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain other drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).

Attenuation of the effect of Duride may occur following concurrent administration of phenytoin.

Concomitant administration of carbamazepine or aminoglutethimide may increase the risk of hyponatraemia.

Corticosteroids administered concurrently may cause sodium retention.

Corticosteroids, carbenoxolone, liquorice, B2 sympathomimetics in large amounts, and prolonged use of laxatives, reboxetine and amphotericin may increase the risk of developing hypokalaemia.

Probenecid, methotrexate and other drugs which, like furosemide, undergo significant renal tubular secretion may reduce the effect of Duride. Conversely, furosemide may decrease renal elimination of these drugs. In case of high-dose treatment (in particular, of both furosemide and the other drugs), this may lead to increased serum levels and an increased risk of adverse effects due to furosemide or the concomitant medication.

Impairment of renal function may develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins.

Concomitant use of ciclosporin and furosemide is associated with increased risk of gouty arthritis.

Risperidone: Caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide or with other potent diuretics should be considered prior to the decision to use. Special warnings and precautions for use regarding increased mortality in elderly patients with dementia concomitantly receiving risperidone.

ADVERSE EFFECTS:
Blood and lymphatic system disorders:
Eosinophilia, haemoconcentration.
Occasionally, thrombocytopenia may occur. In rare cases, leucopenia and, in isolated

cases, agranulocytosis, aplastic anaemia or haemolytic anaemia may develop.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Nervous system disorders
Paraesthesia may occur.
Hepatic encephalopathy in patients with hepatocellular insufficiency may occur.
Dizziness, fainting, loss of consciousness and headache.

Metabolism and nutrition disorders
Serum calcium levels may be reduced; in very rare cases tetany has been observed.

Blood cholesterol and blood triglyceride levels may increase during furosemide treatment. During long term therapy they will usually return to normal within six months.

Glucose tolerance may be impaired with furosemide. In patients with diabetes mellitus this may lead to a deterioration of metabolic control; latent diabetes mellitus may become manifest.

Electrolyte disturbances, metabolic alkalosis increase electrolyte deficit, metabolic acidosis, thirst, headache, hypotension, confusion, muscle cramps, tetany, muscle weakness, disorders of cardiac rhythm and gastrointestinal symptoms. Pseudo-Bartter syndrome, hypovolaemia and dehydration, increases in blood creatinine and blood uric acid, hyponatremia, hypochloremia, hypokalaemia, attacks of gout, hypocalcemia, hypomagnesemia and increased blood urea.

Ear and labyrinth disorders.
Hearing disorders, although usually transitory, may occur in rare cases, particularly in patients with renal failure, hypoproteinaemia (e.g. in nephritic syndrome) and/or when intravenous furosemide has been given too rapidly.Tinnitus, deafness, sometimes irreversible, have been reported after administration of furosemide.

Vascular disorders
Furosemide may cause a reduction in blood pressure (hypotension) which, if pronounced may cause signs and symptoms such as impairment of concentration and reactions, light-headedness, sensations of pressure in the head, headache, dizziness, drowsiness, weakness, disorders of vision, dry mouth, orthostatic intolerance, Thrombosis, Vasculitis.

Hepato-biliary disorders
In isolated cases, intrahepatic cholestasis, an increase in liver transaminases or acute pancreatitis may develop.

Skin and subcutaneous tissue disorders
The incidence of allergic reactions, such as skin rashes, photosensitivity, fever or shock is very low, but when these occur treatment should be withdrawn. Skin and mucous membrane reactions may occasionally occur, e.g. pruritis, urticaria, rashes, dermatitis bullous, erythema multiforme, pemphigoid, dermatitis exfoliative, purpura, photosensitivity, Stevens-Johnson syndrome, toxic epidermal necrolysis, AGEP (acute generalized exanthematous pustulosis) and DRESS (Drug rash with eosinophilia and systemic symptoms), lichenoid reactions.

Psychiatric disorders
Rare complications may include minor psychiatric disturbances.

Renal and urinary disorders
Increased urine volume may provoke or aggravate complaints in patients with an obstruction of urinary outflow. Urine sodium increased, urine chloride increased, urine retention with possible secondary complications may occur. For example, in patients with bladder-emptying disorders, prostatic hyperplasia or narrowing of the urethra. Nephrocalcinosis / Nephrolithiasis has been reported in premature infants, Tubulointerstitial nephritis, Renal failure.

Reproductive system and breast disorders
If furosemide is administered to premature infants during the first weeks of life, it may increase the risk of persistence of patent ductus arteriosus.

Immune system disorders
Severe anaphylactic or anaphylactoid reactions (e.g. with shock) occur rarely, Exacerbation or activation of systemic lupus erythematosus.

Gastrointestinal disorders
Side effects of a minor nature such as nausea, malaise or gastric upset (vomiting or diarrhoea) and constipation may occur but are not usually severe enough to necessitate withdrawal of the treatment, Acute Pancreatitis.

USE IN PREGNANCY AND LACTATION:
Pregnancy:
Furosemide crosses the placental barrier. It must not be given during pregnancy unless there are compelling medical reasons. Treatment during pregnancy requires monitoring of foetal growth.
The safety of Amiloride Hydrochloride has not been established and is therefore not recommended for use during pregnancy.

Lactation:
Furosemide passes into breast milk and may inhibit lactation. It is not known whether Amiloride Hydrochloride is excreted in breast milk. Breastfeeding must be avoided during treatment with Duride.

OVERDOSE:
Treatment of overdosage should be aimed at reversing dehydration and correcting electrolyte imbalance, particularly hyperkalaemia. If hyperkalaemia is seen, appropriate measures to reduce serum potassium must be instituted. Emesis should be induced or gastric lavage performed. Treatment is symptomatic and supportive.

SHELF LIFE
3 years

STORAGE AND INSTRUCTIONS:
Dosage: As directed by the physician.
Instruction: Protect from heat, sunlight & moisture, store below 30°C.
The expiration date refer to the product correctly stored at the required condition.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
Keep out of the reach of children.
To be sold on prescription of a registered medical practitioner only.

PRESENTATION:
Box of 2x10's tablets in blisters.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
Bosch Pharmaceuticals (Pvt) Ltd.
221-223, Sector 23, Korangi Industrial Area,
Karachi - Pakistan

Bosch

For Medical Professional only

Duride® Tablets

(Co-amilofruse)

(Product Specs.: B.P.)

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(کوایمیلوفروز)

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PHARMACEUTICAL COMPANY