PRESCRIBING INFORMATION

AVA-HYDROCHLOROTHIAZIDE

Hydrochlorothiazide Tablets USP

25 and 50 mg

Diuretic – Antihypertensive

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Hydrochlorothiazide Tablets USP

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THERAPEUTIC CLASSIFICATION

Diuretic - Antihypertensive

ACTIONS AND CLINICAL PHARMACOLOGY

Hydrochlorothiazide inhibits reabsorption of sodium and chloride in the distal tubule thus promoting water loss. The higher urine volume increases potassium loss; this loss can often be decreased by restricting sodium intake. Oral doses are well absorbed and reach peak effect in about 4 hours, with a 6 to 12 hour duration. It is excreted unchanged in the urine with a half life of 3 to 5 hours.

The mild blood pressure reducing effects are initially due to volume reduction but the persisting effect includes other undetermined mechanisms that reduce peripheral resistance. A high salt intake reverses its antihypertensive effect.

INDICATIONS AND CLINICAL USE

Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, in drug induced edema (corticosteroid and estrogen therapy) and in edema of renal origin (i.e. nephrotic syndrome, acute glomerulonephritis, chronic renal disease).

In the management of hypertension, hydrochlorothiazide may be used alone or as an adjunct to other antihypertensive drugs. Since it enhances the action of these agents, their dosage must be reduced to avoid an excessive drop in blood pressure and other adverse effects.

CONTRAINDICATIONS

Anuria; discontinue if increasing azotemia and oliguria occur during treatment of severe progressive renal disease. Do not use in patients known to be sensitive to thiazides or other sulfonamide derived drugs.

PRECAUTIONS

May precipitate or increase azotemia; cumulative effects may develop in presence of impaired renal function; discontinue if increasing azotemia and oliguria occur during treatment of severe progressive renal disease. Use with caution in impaired hepatic function or progressive liver disease since minor alterations of fluid and electrolyte balance or of serum ammonia may precipitate hepatic coma.

The possibility of sensitivity reactions should be considered 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.

Check carefully for signs of fluid and electrolyte imbalance, namely hyponatremia, hypochloremic alkalosis and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient has other disorders that predispose to fluid and

electrolyte imbalance such as vomiting, diarrhea, heart failure, liver or renal disease, is on a salt-restricted diet, or is receiving parenteral fluids. The elderly may be at greater risk for developing electrolyte abnormalities, including hypomagnesemia, due to age-related changes in renal function. Warning signs, irrespective of cause, are: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances.

Prevent or treat hypokalemia with foods high in potassium, or, if necessary, with supplemental potassium chloride.

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.

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 or hypochloremic alkalosis.

Should hypochloremic alkalosis or hyponatremia occur, withdrawal of the diuretic, fluid restriction and other appropriate therapy should be considered.

Pathological changes in the parathyroid glands with hypercalcemia and hypophosphatemia have been observed in a few patients on prolonged thiazide therapy. The common complications of hyperparathyroidism such as renal lithiasis, bone resorption, and peptic ulceration have not been seen. Discontinue thiazides before carrying out parathyroid function tests.

Caution is necessary in patients with hyperuricemia or a history of gout since gout may be precipitated.

Drug Interactions

Hypokalemia may develop (especially with brisk diuresis) in severe cirrhosis; with concomitant steroid or ACTH therapy; or with inadequate electrolyte intake. Hypokalemia can sensitize or exaggerate the response of the heart to toxic effects of digitalis.

Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the drug may be enhanced in the post sympathectomy patient.

Insulin or oral hypoglycemic dosage requirements may be altered by thiazides. Latent diabetes mellitus may become manifest.

Hydrochlorothiazide may add to or potentiate the action of other antihypertensive drugs, and decrease responsiveness to norepinephrine.

Diuretics enhance the cardiotoxic (e.g. ECG changes) and neurotoxic (e.g. ataxia, confusion and mental disorientation) effects of lithium and these drugs should ordinarily not be administered concurrently. In those rare instances when these drugs must be given together, patients should be observed closely for signs and symptoms of lithium toxicity. Close monitoring of serum electrolytes and lithium concentrations and maintenance of adequate fluid, potassium and sodium intake also are necessary.

Pregnancy

The routine use of thiazide diuretics in an otherwise healthy pregnant woman with or without edema is not appropriate. Edema in pregnancy, resulting from restriction of venous return by the expanded uterus, is treated though elevation of the lower extremities and use of support hose. A short course of diuretics may be appropriate in patients with severe hypervolemia not relieved by rest or these measures. Pathological edema such as cardiac, nephrotic or hepatic edema may be an indication for use of thiazide diuretics. Thiazides do not prevent toxemia of pregnancy, nor are they useful in its treatment.

Thiazides cross the placental barrier. Possible risks include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions that have occurred in the adult.

Lactation

Thiazides are excreted into the milk of nursing women, although apparently not in significant amounts. The potential for idiosyncratic or allergic reaction in the infant should be considered. It should be noted that diuretics may partially inhibit lactation.

ADVERSE REACTIONS

Gastrointestinal: Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis, sialadenitis.

CNS: Dizziness, vertigo, paresthesias, headache, xanthopsia.

Hypersensitivity: Purpura, photosensitivity, rash, urticaria, necrotizing angiitis, fever, respiratory distress including pneumonitis, anaphylactic reactions.

Hematologic: Leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia, hemolytic anemia.

Cardiovascular: Orthostatic hypotension may occur, especially in elderly patients with reduced plasma volume and may be potentiated by alcohol, barbiturates or narcotics.

Miscellaneous: Muscle spasm, weakness, restlessness, hyperglycemia, glycosuria, hyperuricemia, transient blurred vision. Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms

Overdosage may lead to excessive diuresis with electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration. If digitalis has also been administered, hypokalemia may accentuate myocardial abnormalities (e.g. cardiac arrhythmias).

Signs are dry mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, gastrointestinal disturbances, mental confusion, delirium, convulsions, shock, coma.

Treatment

There is no specific antidote. If ingestion is recent, gastric lavage or emesis may reduce absorption; activated charcoal may be given. Otherwise, management includes symptomatic treatment with special attention to cardiac rate and output, blood volume, electrolyte balance, dehydration, paralytic ileus, urinary function, hepatic coma, and cerebral activity. Administration of sympathomimetic drugs (e.g. dopamine) may be indicated. Administer oxygen or artificial respiration for respiratory impairment.

DOSAGE AND ADMINISTRATION

Diuresis

The usual adult dose is 25 to 200 mg per day; the maintenance dose is 25 to 100 mg per day, depending on patient response. Some patients may respond to intermittent therapy (alternate days or 3 to 5 days per week). The usual oral dosage for children is 2 mg/kg per day, given in 2 divided doses. Infants under 6 months of age may require up to 3 mg/kg per day, in 2 divided doses.

Hypertension

Doses as low as 12.5 mg daily may be effective, especially in the elderly. Usual adult dose is 25 to 50 mg daily. Doses above this level may increase effectiveness very little but cause more side effects such as hypokalemia. In hypertension associated with renal failure volume overload, more potent diuretics, such as loop diuretics may have to be used.

AVAILABILITY OF DOSAGE FORMS

25 mg: Each round, pale pink, flat-faced with bevelled edge tablet, scored and identified APO over 25, contains hydrochlorothiazide 25 mg. Available in bottles of 100 and 1000.

50 mg: Each round, pale pink, flat-faced with beveled edge tablet, scored and identified APOR over 50, contains hydrochlorothiazide 50 mg. Available in bottles of 100.