

Hydrene 25/50

Hydrochlorothiazide/Triamterene



PRODUCT INFORMATION

Composition

Each tablet contains triamterene 50 mg, hydrochlorothiazide 25 mg.

Description

Triamterene is 2,4,7-triamino-6-phenylpteridine. Hydrochlorothiazide is 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1.1-dioxide.

Actions

Hydrene is an oral diuretic/antihypertensive agent that combines two natriuretics, each of which complements the action of the other.

Pharmacology

The hydrochlorothiazide component blocks reabsorption of sodium and chloride ions and thereby increases the quantity of sodium traversing the distal tubule and the volume of water excreted. A portion of the additional sodium presented to the distal tubule is exchanged there for potassium and hydrogen ions. With continued use of hydrochlorothiazide and depletion of sodium, compensatory mechanisms tend to increase this exchange and may produce excessive loss of potassium and hydrogen ions.

The triamterene component exerts its diuretic effect on the distal renal tubule to inhibit the reabsorption of sodium in exchange for potassium and hydrogen ions. By inhibiting the distal tubular exchange mechanism, triamterene maintains or increases the sodium excretion and reduces the excess loss of potassium and hydrogen ions induced by hydrochlorothiazide.

The duration of diuretic activity and effective dosage range of the hydrochlorothiazide and triamterene components of Hydrene are similar. Diuretic activity following a single dose is evident within the first hour, reaching a peak at 2 to 3 hours, and tapering off during the next 7-9 hours.

Pharmacokinetics

Metabolism and excretion. Both components of Hydrene are rapidly absorbed from the gastrointestinal tract. The absorption of the triamterene component, however, is variable and 10 to 88% of an oral dose may be recovered in the urine in 24 hours. About 67% of the absorbed triamterene is bound to plasma proteins. Renal excretion is due both to filtration and tubular secretion.

The elimination half-life of hydrochlorothiazide is approximately 3 to 6 hours; it is probably actively secreted in the proximal tubule.

Indications

Treatment of oedema associated with congestive heart failure, hepatic cirrhosis and the nephrotic syndrome; corticosteroid and oestrogen induced oedema and idiopathic oedema.

Treatment of mild to moderate hypertension when the potassium sparing action of triamterene is warranted (thiazide-like diuretics cause hypokalaemia) and in those patients in whom potassium depletion is considered especially dangerous (e.g. digitalised patients). It can be used alone or in combination with other antihypertensive drugs.

Contraindications

Hydrene should not be given to patients receiving other potassium conserving agents such as spironolactone, amiloride or other formulations containing triamterene. Concomitant potassium containing salt substitutes should also not be used. Potassium supplementation should not be used with Hydrene except in severe cases of hypokalaemia. Such concomitant therapy can be associated with rapid increases in serum potassium levels. If potassium supplementation is used, careful monitoring of the serum potassium level is necessary. Hydrene is contraindicated in patients with anuria, acute and chronic renal insufficiency or significant renal impairment, increasing oliguria and azotaemia. Hypersensitivity to either drug in the preparation or to other sulfonamide derived drugs. Hydrene should not be used in patients with pre-existing elevated serum potassium. Hepatic dysfunction.

Warnings

Because of the potassium conserving effect of triamterene, hypokalaemia is an uncommon occurrence with the use of Hydrene. Patients should not be placed on dietary potassium supplements or potassium salts in conjunction with Hydrene unless they develop hypokalaemia or their dietary intake of potassium is markedly impaired.

Hyperkalaemia (> 5.4 mEq/L) is more likely to occur in patients with renal impairment, diabetes (even without evidence of renal impairment) and elderly or severely ill patients. Hyperkalaemia has been reported ranging in incidence from 4% in patients less than 60 years to 12% in patients 60 and older, with an overall incidence of less than 8%. Rare cases have been associated with cardiac irregularities. Since uncorrected hyperkalaemia may be fatal, serum potassium levels must be monitored at frequent intervals, especially in patients first receiving Hydrene, when dosages are changed or with any illness that may influence renal function. In those patients who develop hyperkalaemia, Hydrene should be withdrawn and a thiazide alone substituted.

Patients should be observed regularly for the possible occurrence of blood dyscrasias, hepatic damage or other idiosyncratic reactions. There have been reports of blood dyscrasias in patients receiving triamterene. Leucopenia, thrombocytopenia, agranulocytosis and aplastic anaemia have been reported in rare instances with the thiazides.

Periodic plasma urea and serum potassium determinations should be made to check renal function, especially in elderly patients and in patients with suspected or confirmed renal or hepatic insufficiency.

Hepatic coma may result from electrolyte imbalance in acutely ill cirrhotic patients. As with the use of any diuretic, the physician should proceed cautiously in such patients and be alert for early signs of impending coma such as confusion, drowsiness and tremor.

Lithium generally should not be given with diuretics because they reduce its renal clearance and increase the risk of lithium toxicity.

Precautions

Electrolyte imbalance, often encountered in such diseases as heart failure, renal disease or cirrhosis of the liver, may also be aggravated or caused independently by any diuretic agent including Hydrene. Since Hydrene is a combination of two potent diuretics, the possibility of electrolyte imbalance should be kept in mind when using high doses for prolonged periods or in patients on a salt restricted diet. Periodic serum electrolyte determinations should be performed during therapy.

Hydrene may produce an elevated blood urea nitrogen level, creatinine level or both. This apparently is secondary to a reversible reduction of glomerular filtration rate or a depletion of intravascular fluid volume, rather than renal toxicity. If azotaemia increases, discontinue Hydrene.

Cirrhotics with splenomegaly may have marked variations in their blood pictures, including thrombocyte and leucocyte levels, which are not related to drug therapy. Periodic blood studies in these patients are recommended.

Since Hydrene has an antihypertensive effect, its use with another antihypertensive drug requires reduced dosage of the latter agent. When Hydrene is added to another antihypertensive already being used as therapy, the dose of the other antihypertensive drug should be reduced at least by half. Subsequent adjustment of dosage should be made as required. The antihypertensive effects of Hydrene may be enhanced in the postsympathectomy patient.

Hydrene, because of its hydrochlorothiazide component, may cause hyperglycaemia and glycosuria. In diabetics, the insulin requirement may be altered.

Hyperuricaemia may be observed with possible occurrence of gout. However, Hydrene does not appear to offer greater liability than that reported for hydrochlorothiazide alone. Triamterene may cause a decreasing alkali reserve with the possibility of metabolic acidosis.

Thiazides have been shown to decrease arterial responsiveness to noradrenaline and to increase the paralysing effect of tubocurarine; consequently, caution should be observed in patients undergoing surgery.

Triamterene has been reported, in higher doses, to increase the incidence of renal stones.

Use in Pregnancy (Risk Category: C)

Hydrochlorothiazide. Thiazides, related diuretics and loop diuretics enter the fetal circulation and may cause electrolyte disturbances. Neonatal thrombocytopenia has been reported with thiazides and related diuretics. Loop diuretics like frusemide and bumetanide are probably also associated with this risk. During the latter part of pregnancy, products of this type should only be given on sound indications, and then in the lowest effective dose.

The possibility of fetal or neonatal jaundice, thrombocytopenia or pancreatitis during the use of thiazides in pregnant women should be considered.

Triamterene. Passive transfer of these drugs across the human placenta has been demonstrated. Maternal treatment during pregnancy may result in electrolyte disturbances in the fetus.

Use in Lactation

Thiazides appear and triamterene may appear in breast milk. If use of Hydrene is deemed essential, the patient should stop nursing.

Use in Children

Adequate information on the use of Hydrene in children is not available.

Interactions

Hydrene should not be given to patients receiving other potassium sparing agents. Angiotensin converting enzyme (ACE) inhibitors can also elevate serum potassium levels; the co-administration of these agents with Hydrene should be undertaken with caution.

Triamterene is less likely to cause marked hypokalaemia than the thiazide diuretics, but if depletion of serum potassium occurs with Hydrene, the toxicity of digitalis glycosides and nondepolarising muscle relaxants may be enhanced; the hypotensive effects of CNS depressants such as phenothiazines, MAOIs and antihypertensive agents such as guanethidine, methyldopa, rauwolfia alkaloids and hydralazine may be potentiated; thiazides may potentiate the hypoglycaemic effects of oral sulphonylureas, but triamterene has been reported to inhibit these compounds; triamterene may also potentiate methotrexate.

Concurrent use with chlorpropamide may increase the risk of severe hyponatraemia.

Triamterene and quinidine have similar fluorescence spectra; thus, Hydrene will interfere with the fluorescent measurement of quinidine.

A possible interaction resulting in acute renal failure has been reported in a few patients on triamterene/hydrochlorothiazide preparations when treated with indomethacin and therefore, particular care should be exercised in patients receiving NSAIDs and potassium sparing agents like triamterene.

Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics. The use of an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist), an anti-inflammatory drug (NSAID or COX-2 inhibitor) and a thiazide diuretic at the same time increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.

Adverse Reactions

Hypersensitivity. Anaphylaxis, rash, urticaria, photosensitivity.

Cardiovascular. Arrhythmias, postural hypotension.

Metabolic. Diabetes mellitus, hyperkalaemia, hyperglycaemia, glycosuria, hyperuricaemia, hypokalaemia, hyponatraemia, acidosis, hypochloraemia.

Gastrointestinal. Jaundice and/or liver enzyme abnormalities, pancreatitis, nausea and vomiting, diarrhoea, constipation, abdominal pain.

Renal. Acute renal failure, interstitial nephritis, renal stones composed primarily of triamterene, elevated BUN and serum creatinine, abnormal urinary sediment.

Haematological. Leucopenia, thrombocytopenia and purpura, megaloblastic anaemia.

Musculoskeletal. Muscle cramps.

Central nervous system. Weakness, fatigue, dizziness, headache, dry mouth.

Miscellaneous. Impotence, sialadenitis.

Thiazides alone have been shown to cause the following additional adverse reactions.

Central nervous system. Paraesthesias, vertigo.

Ophthalmic. Xanthopsia, transient blurred vision.

Respiratory. Allergic pneumonitis, pulmonary oedema, respiratory distress.

Other. Necrotising vasculitis, exacerbation of lupus.

Haematological. Aplastic anaemia, agranulocytosis, haemolytic anaemia.

Thrombocytopenia and pancreatitis occur rarely in newborns whose mothers have received thiazides during pregnancy.

Dosage and Administration

Adults. (Adequate information of the use of Hydrene in children is not available. Therefore, only adult dosage is given).

It should be appreciated that in oedema or hypertension, therapy needs to be titrated to the individual patient and must be re-evaluated as conditions in each patient warrant.

Hypertension. Initially 1 tablet daily after the morning meal, thereafter adjusted to the patient's needs, not exceeding a maximum of 4 tablets daily.

When changing from other diuretics or antihypertensives to Hydrene, simply stop the previous therapy and start Hydrene at the appropriate dosage within the recommended dosage range. Since Hydrene has an antihypertensive effect, its use with another antihypertensive drug requires reduced dosage of the latter agent. When Hydrene is added to another antihypertensive already being used as therapy, the dosage of the other antihypertensive drug should be reduced at least by half. Subsequent adjustment of dosage should be made as required.

Oedema. The usual starting dosage is 1 tablet twice daily after meals.

When adequate control of oedema has been achieved, the patient may be maintained on 1 tablet daily; in some patients, 1 tablet every other day may be sufficient. The maximum total daily dosage should not exceed 1 tablet four times daily; however, at this dosage, the incidence of side effects may increase.

Warning. Patients should not be given dietary potassium supplements or potassium salts in conjunction with Hydrene unless they develop hypokalaemia or their dietary intake of potassium is markedly impaired.

Overdosage

Symptoms. Electrolyte imbalance is the major concern. Symptoms reported include polyuria, nausea, vomiting, weakness, lassitude, fever, flushed face and hyperactive deep tendon reflexes.

Treatment. If hypotension occurs, it may be treated with pressor agents such as noradrenaline to maintain blood pressure. Carefully evaluate the electrolyte pattern and fluid balance. Induce immediate evacuation of the stomach through emesis or gastric lavage. There is no specific antidote.

Presentation

Hydrene 25/50, Hydrochlorothiazide 25 mg with triamterene 50 mg tablet: yellow, marked "T" breakline "H" on one side and "α" on the reverse; 100's.

Poison Schedule

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Approved by the Therapeutic Goods Administration on 18 September 1992.

Date of most recent amendment: 8 June 2005.