

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dytide Capsules

Benzthiazide 25mg and Triamterene 50mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 50 mg Triamterene Ph. Eur. and 25 mg Benzthiazide USP.

3. PHARMACEUTICAL FORM

Clear, colourless capsules with opaque, maroon caps, containing a yellow granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Potassium-conserving diuretic preparation for the control of oedema in cardiac failure, cirrhosis of the liver or nephrotic syndrome, and in that associated with corticosteroid treatment.

4.2 Posology and method of administration

Method of Administration:

Oral.

Dosage:

Adults Only: The optimal dosage is 3 Dytide Capsules a day, 2 being taken after breakfast and 1 after lunch. After the first week, treatment should preferably be given on alternative days, to ensure satisfactory maintenance diuresis without an increase in blood urea levels. Maintenance dosage may be

reduced to 1 or 2 capsules every other day, taken after breakfast or after breakfast and lunch.

Elderly: A lower dosage may be sufficient. The normally occurring reduction in glomerular filtration with age must be borne in mind.

4.3 Contraindications

Hyperkalaemia, progressive renal failure, increasing hepatic dysfunction, hypercalcaemia, diabetic ketoacidosis, Addison's disease, known hypersensitivity to either constituent of the product. Routine concomitant administration of potassium supplements, or other potassium-conserving drugs, including ACE inhibitors.

4.4 Special warnings and precautions for use

Use with caution in patients with hepatic or renal insufficiency; in those predisposed to gout, since both components can elevate uric acid levels; with hypotensive agents since an additive effect may result; in diabetic patients since thiazides can provoke hyperglycaemia and glycosuria; in diabetic nephropathy due to increased risk of hyperkalaemia.

It is advisable to monitor blood urea, serum potassium levels and electrolytes periodically. This is important in the elderly, those with renal impairment and those receiving concomitant treatment with NSAID's. Triamterene and thiazides reduce excretion of lithium and may thus precipitate intoxication. Very rare cases of SLE have been reported associated with triamterene and hydrochlorothiazide.

Aggravation of pancreatitis may also occur. Combinations of folate antagonists and triamterene are not advisable in pregnancy or in patients with cirrhosis because of the increased theoretical risk of folate deficiency developing.

Dytide Capsules may cause the urine to be coloured fluorescent blue.

Photosensitivity has been reported quite frequently with treatments containing triamterene. Patients must be advised about this side effect and to take adequate precautions.

4.5 Interactions with other medicinal products and other forms of interaction

Interactions with other drugs have to be considered:

- Tubocurrarine-increased response to this relaxant.

- Colestyramine/Colestipol-absorption of Dytide reduced
- Insulin-Dytide antagonises the hypoglycaemic effect of insulin.
- Combined oral contraceptives-Dytide effect is reduced.

Increased hypotensive effect of Dytide by:

- Dipyridamole
- Alprostadl
- Moxisylyte
- Tizanidine
- Beta blocker eye drops
- MAOI's

Increased postural hypotensive effect of Dytide by:

- First dose of alpha blocker
- Alpha blockers

Increased risk of hypercalcaemia by:

- Parenteral calcium
- Oral calcium salts

Increased risk of hyperkalaemia by:

- ACE inhibitors
- ACE inhibitors with thiazides
- Angiotensin inhibitors
- Ciclosporin
- Potassium salts
- Tacrolimus
- Trilostane
- Indomethacin

Increased risk of hypersensitivity-Allopurinol

Increased risk of hyponatraemia with:

- Chlorpropamide
- Aminoglutethimide
- Carbamazepine

Increased risk of nephrotoxicity and antagonism of diuretic effect - NSAID's

Increased risk of postural hypotension - Tricyclic antidepressants

Increased risk of renal failure - Indomethacin

- Lithium-increased risk of lithium toxicity
- Drospirenone-may increase risk of hyperkalaemia
- Metfuran, Repaglinide/Nateglinide, Sulphonylureas, Troglitazone-reduced hypoglycaemic effect

Dytide Capsules are contraindicated in pregnancy and breast-feeding.

4.6 Pregnancy and lactation

Animal studies have not suggested foetal abnormalities. Nevertheless, both triamterene and thiazides have been shown to pass through the placenta in humans and also to pass into breast milk. In rare instances, thrombocytopenia, pancreatitis or hypoglycaemia have been reported in new-born infants of mothers treated with thiazides. Dytide is best avoided in pregnancy unless for used for a pre-existing illness and then only after assessing risk versus benefit. It should not be used in breast feeding mothers.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Nausea, vomiting, diarrhoea, muscle cramps, weakness, dizziness, headache, dry mouth, thirst, decreases in blood pressure, and rash have all been reported. Photosensitivity is very rare. Anaphylaxis is a remote possibility. Minor serum electrolyte changes have been observed infrequently, and marked fluctuations in serum potassium levels are uncommon. Metabolic acidosis occasionally occurs. Hyperglycaemia, increased uric acid levels which sometimes lead to gout, and hypercalcaemia that does not lead to tertiary hyperparathyroidism may also occur. Electrolyte imbalance may also indicate excessive dosage or be secondary to the condition under treatment. In common with most diuretics, Dytide may reduce glomerular filtration rate and cause a temporary increase in blood urea and creatinine levels; again this may also indicate excessive dosage or be secondary to the condition under treatment. It can also cause increases in plasma lipid levels.

Renal failure, reversible on stopping treatment, has been reported very rarely and has been due to acute interstitial nephritis or an interaction between triamterene and some NSAID's. Triamterene has been found in renal stones both alone and in association with other usual calculus components. There is no evidence that stone formation is increased in patients taking triamterene-containing drugs.

Rare cases of thrombocytopenic purpura and megaloblastic anaemia have been reported with triamterene; thiazides alone have caused jaundice and acute pancreatitis and, rarely blood dyscrasias including agranulocytosis, thrombocytopenia and leucopenia. Very rare cases of SLE have been reported associated with combined triamterene and hydrochlorothiazide.

4.9 Overdose

Symptoms of electrolyte imbalance, especially hyperkalaemia, are likely. Symptoms include nausea, vomiting, weakness, lassitude, muscular weakness, hypotension and cardiac arrhythmias. Treatment consists of gastric lavage with careful monitoring of electrolytes and fluid balance. Cardiac rhythm should be monitored and appropriate measures taken to correct hyperkalaemia as necessary. There is no specific antidote. There may be some benefit to renal dialysis in cases of severe overdosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Triamterene is a potassium conserving diuretic thought to act by directly inhibiting the exchange of sodium for potassium and hydrogen in the distal renal tubule.

Benzthiazide is a thiazide diuretic which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excreting of sodium and chloride ions, and consequently of water. Potassium ions are excreted to a lesser extent.

5.2 Pharmacokinetic properties

Onset of diuresis takes place within one hour, peaks at 2-3 hours and tapers off during the subsequent 7-9 hours.

Triamterene is incompletely but fairly rapidly absorbed from the gastro-intestinal tract. It has been estimated to have a plasma half-life of about 2 hours. It is extensively metabolised and is mainly excreted in the form of metabolites with some unchanged triamterene; variable amounts are also excreted in the bile.

Benzthiazide is poorly absorbed from the gastro-intestinal tract, and is excreted almost entirely unchanged in the urine.

5.3 Preclinical safety data

No further information of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate
Lactose

Hard Gelatin Capsule:
Erythrosine E127
Indigo Carmine E132
Titanium Dioxide E171

6.2 Incompatibilities

None known.

6.3 Shelf life

Polypropylene securitainers, amber glass bottle, polyethylene vials = 60 months
PVC blister packs = 36 months

6.4 Special precautions for storage

Store in a dry place.

6.5 Nature and contents of container

Polypropylene securitainers, amber glass bottles containing 30 capsules.
Polyethylene vials containing 250 capsules.
PVC blister packs containing 30 capsules.

6.6 Instruction for use, handling and disposal

None

ADMINISTRATIVE DATA

7. MARKETING AUTHORISATION HOLDER

Goldshield Group Plc
NLA Tower
Croydon
CR0 0XT

Trading as: Goldshield Pharmaceuticals

8. MARKETING AUTHORISATION NUMBER

PL 10972/0018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

24th December 1993

10. DATE OF REVISION OF THE TEXT

10/09/2007