

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

Dyazide 50mg/25mg Tablets

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 50mg triamterene and 25mg hydrochlorothiazide.

### **3. PHARMACEUTICAL FORM**

Peach-coloured, half-scored, circular tablets bearing the mark E93.

### **4. CLINICAL PARTICULARS**

#### **4.1. Therapeutic indications**

Dyazide is a potassium-conserving diuretic preparation with antihypertensive activity. It is recommended for the treatment of mild to moderate hypertension, alone or in combination with other antihypertensive drugs. It is also indicated in 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**

*Adults Only:* In Hypertension: Initially one tablet a day after the morning meal, thereafter adjusted to the patient's needs. If 'Dyazide' is added to already established therapy with another antihypertensive drug, the dosage of the latter should be reduced, and later adjusted if necessary. If another antihypertensive drug is added to 'Dyazide' therapy, the dosage of the latter will not normally be reduced.

*Adults Only:* In Oedema: The usual starting dose is one 'Dyazide' tablet twice a day after meals. The optimal dosage may be 3 tablets a day, two after breakfast and one after lunch. Maintenance Dosage: Once a diuresis has been established, dosage should be reduced. Usually one tablet a day, or two tablets on alternate days, will suffice.

A dosage of 4 tablets a day should not be exceeded; at this level adverse reactions such as raised blood urea are more likely.

*Elderly:* Dosage as above. 'Dyazide' has been widely used and is usually well tolerated in patients over the age of 60 years. The normally occurring reduction in glomerular filtration with age should be borne in mind.

*Children:* Only limited information is available on the use of 'Dyazide' in children and, therefore its use in children is not recommended.

### **4.3 Contra-indications**

Do not give 'Dyazide' to patients with hyperkalaemia, progressive renal failure, increasing hepatic dysfunction, hypercalcaemia, diabetic ketoacidosis, Addison's disease or known hypersensitivity to either constituent of the product. Potassium supplements, or other potassium-conserving drugs, including ACE inhibitors, should not be given routinely with 'Dyazide'.

### **4.4. Special warnings and special precautions for use**

Use 'Dyazide' with caution in patients with hepatic or renal insufficiency, and in those predisposed to gout, since both components can elevate uric acid levels. Use with caution with hypotensive agents since an additive effect may result. Since thiazide diuretics can provoke hyperglycaemia and glycosuria; diabetic patients should be treated with care, as should patients with 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 NSAIDs (see section 4.8).

Triamterene and thiazides reduce excretion of lithium and may thus precipitate intoxication.

Very rare cases of systemic lupus erythematosus (SLE) have been reported associated with 'Dyazide'. Pancreatitis may be aggravated.

Combinations of folate antagonists and triamterene are not advisable in pregnancy or in patients with hepatic cirrhosis because of the increased theoretical risk of folate deficiency developing.

Triamterene may cause a blue fluorescence of the urine under certain light conditions.

'Dyazide' interferes with some laboratory tests of thyroid and parathyroid functions, and bioassay of folic acid.

No Data Held

#### **4.5. Interactions with other medicinal products and other forms of interaction**

*Analgesics:* It is advisable to monitor blood urea and serum potassium levels periodically in patients receiving concomitant treatment with NSAIDs. Renal failure, reversible on stopping treatment, has been reported very rarely which may be due to a reaction between triamterene and some NSAIDs. There have been occasional reports of decreased renal function when indometacin is given with triamterene, hence concomitant use should be avoided. NSAIDs may also antagonise the diuretic action of triamterene and hydrochlorothiazide. An increased risk of hyperkalemia also exists when NSAIDs are used concomitantly with triamterene.

*Anion Exchange Resins:* Colestyramine and colestipol reduce the absorption of thiazides and if administered should be taken at least two hours apart.

*Antidepressants:* When co-administered with reboxetine there is an increased risk of hypokalaemia. There is an increased risk of postural hypotension with tricyclics. An enhanced hypotensive effect may also occur when given in conjunction with MAOIs.

*Antidiabetics:* Hypoglycaemic effect may be antagonised by thiazide diuretics. Chlorpropamide increases the risk of hyponatraemia associated with thiazides in combination with potassium sparing diuretics. When used in conjunction with sulphonylureas, the dosage of the hypoglycaemic agent may require upward adjustment.

*Antifungals:* There is an increased risk of hypokalaemia if thiazides are given with amphotericin. Hydrochlorothiazide increases the plasma concentration of fluconazole.

*Antihypertensives:* 'Dyazide' may enhance the effect of other antihypertensive drugs. There is an enhanced hypotensive effect and an increased risk of first-dose hypotensive effect of post-synaptic alpha-blockers such as prazosin. 'Dyazide' should be used with caution in conjunction with ACE inhibitors or Angiotensin II receptor antagonists due to an increased risk of hyperkalaemia with potassium sparing diuretics.

*Antipsychotics:* Hypokalemia increases risk of ventricular arrhythmias with pimozide or thioridazine (avoid concomitant use) and with amisulpride and sertindole.

*Calcium Salts:* Concurrent administration with thiazides increases the risk of hypercalcaemia.

*Cardiac Glycosides and Antiarrhythmic Drugs:* Increased toxicity if hypokalaemia occurs with thiazide.

*Ciclosporin*: An increased risk of hyperkalemia exists when used with triamterene.

*Corticosteroids*: Use with caution in conjunction with corticosteroids, since an additive effect may result in excess potassium loss and an increased risk of hypokalaemia. Corticosteroids are also reported to antagonise the diuretic effect.

*Cytotoxics*: Increased risk of nephrotoxicity and ototoxicity has been reported with platinum compounds like cisplatin.

*Other Diuretics*: An increased risk of hypokalaemia if acetazolamide, loop diuretics or thiazides are given together.

*Lithium*: Triamterene and thiazides reduce excretion of lithium and may thus precipitate intoxication.

*Muscle Relaxants*: Enhanced hypotensive effect with baclofen and tizanidine.

*Oestrogens and Progestogens*: Oestrogens and combined oral contraceptives antagonise diuretic effect. Possible hyperkalemia may occur with potassium sparing diuretics.

*Potassium Supplements*: An increased risk of hyperkalaemia exists with concomitant triamterene use.

*Sympathomimetics*: There is an increased risk of hypokalaemia if thiazides are taken with high doses of bambuterol, fenoterol, eformoterol, ritodrine, salbutamol, salmeterol and terbutaline.

*Tacrolimus*: Increased risk of hyperkalemia with potassium sparing diuretics.

*Theophylline*: If taken with thiazides, there is an increased risk of hypokalaemia.

*Ulcer Healing Drugs*: Such as carbenoxolone antagonises the diuretic effect concurrent administration with thiazides increases the risk of hypokalaemia.

*Vitamin D*: The risk of hypercalcaemia is increased if thiazides are taken with Vitamin D.

#### **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 newborn infants of mothers treated with thiazides. 'Dyazide' is best avoided in pregnancy unless

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**

There are no known effects of 'Dyazide' on the ability to drive and operate machinery.

#### **4.8. Undesirable effects**

Nausea, vomiting, diarrhoea, muscle cramps, weakness, dizziness, headache, dry mouth, thirst, undesirable decrease in blood pressure, and rash have been reported. Photosensitivity and systemic lupus erythematosus (SLE) have also been rarely reported. Anaphylaxis is a remote possibility.

Minor serum electrolyte changes have been observed infrequently, and marked fluctuations in serum potassium levels are uncommon. Long-term use has confirmed that little change occurs in serum potassium and sodium levels in most patients. Metabolic acidosis occasionally occurs. Electrolyte imbalance may also indicate excessive dosage or be secondary to the condition under treatment. Hyperglycaemia, increased uric acid levels which sometimes lead to gout, and hypercalcaemia that does not lead to tertiary hyperparathyroidism may also occur

In common with most other diuretics, 'Dyazide' 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 NSAIDs.

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, acute pancreatitis and, rarely, blood dyscrasias including agranulocytosis, thrombocytopenia and leucopenia.

Acute interstitial pneumonitis and pulmonary oedema of non-cardiac origin have been reported very rarely.

#### **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. Renal dialysis may be of some benefit in cases of severe overdosage.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1. Pharmacodynamic properties**

The product contains triamterene and hydrochlorothiazide.

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.

Hydrochlorothiazide is a thiazide diuretic which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excretion 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 two to three hours and tapers off during the subsequent seven to nine hours.

Triamterene is incompletely but fairly rapidly absorbed from the gastrointestinal tract. It has been estimated to have a plasma half-life of about two 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.

Hydrochlorothiazide is incompletely but fairly rapidly absorbed from the gastrointestinal tract. It is excreted unchanged in the urine.

### **5.3. Pre-clinical safety data**

Long term carcinogenicity studies have not been conducted with Dyazide, the hydrochlorothiazide /triamterene combination. In two year feeding studies with triamterene in rodents there was some evidence of an increase in the incidence of liver tumours, including carcinoma, in both sexes of mice and in male rats. The relevance of this finding to humans is unknown.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1. List of excipients**

Core:

Maize Starch  
Povidone 30  
Sodium Lauryl Sulphate  
FD & C Yellow No.6 (E110)  
Purified water

Coating:

Maize Starch  
Sodium Starch Glycollate  
Magnesium Stearate

### **6.2. Incompatibilities**

Not applicable.

### **6.3. Shelf life**

'Dyazide' tablets have a shelf-life of five years.

### **6.4. Special precautions for storage**

There are no special storage requirements.

### **6.5. Nature and content of container**

Opaque blister packs containing either 15, 30 or 60 tablets.  
Securitainers, polythene vials or amber glass bottles containing either 20, 100, 500 or 1000 tablets.

**6.6. Instructions for use, handling and disposal**

None.

**ADMINISTRATIVE DATA**

**7. MARKETING AUTHORISATION HOLDER**

Goldshield Pharmaceuticals Ltd  
NLA Tower  
12-16 Addiscombe Road  
Croydon  
Surrey CR0 0XT  
United Kingdom

**8. MARKETING AUTHORISATION NUMBER**

PL 12762/0042

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF  
AUTHORISATION**

8 May 2000

**10. DATE OF REVISION OF THE TEXT**

13/08/2010