Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dyazide 50mg/25mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of Triamterene and 25 mg of Hydrochlorothiazide.

Excipient: Contains 0.12mg of Sunset Yellow (E110) per tablet.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
Peach coloured, compressed, flat circular, bevel-edged tablet with a single scoreline on one surface and the code ‘E93’ on the other.

The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

It is recommended for the treatment of mild to moderate hypertension, alone or in combination with other antihypertensive drugs. It is also recommended in the control of oedema due to cardiac failure, cirrhosis of the liver or the nephrotic syndrome. It can also be used to control the oedema associated with corticosteroid treatment, but only when the concomitant use of diuretics is considered essential.

4.2 Posology and method of administration

Route of administration: oral.

Adults: In hypertension

The recommended dosage is one tablet a day after the morning meal. 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: In oedema

One “Dyazide” tablet a day after the morning meal.

Elderly

Dosage as for adults. “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 (see section 4.4).

4.3 Contraindications

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, spironolactone or amiloride, should not be given routinely with "Dyazide". "Dyazide" should not be used during lactation or in neonates or young infants.

4.4 Special warnings and precautions for use

Use "Dyazide" with caution in patients with hepatic or renal insufficiency or urinary tract obstruction 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, particularly in patients with latent diabetes, and adjustment of the dosage of hypoglycaemic agents may be necessary in diabetic patients. Dosage of concomitant cardiac glycosides may need to be adjusted.

It is advisable to monitor blood urea, serum potassium levels and electrolytes periodically to avoid inadequate potassium supplementation or excessive loss of fluid. 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.

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.

These tablets contain Sunset yellow (E110), which may cause allergic reactions.

4.5 Interaction 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 Angiotensin Converting Enzyme (ACE) inhibitors , spironolactone, amiloride 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 inceases the risk of hypokalaemia.

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

4.6 Fertility, pregnancy and lactation

Animal studies have not suggested foetal abnormalities. Nevertheless, Bboth 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. ‘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, hypersensitivity reactions and rash have been reported. Photosensitivity and systemic lupus erythematosus (SLE) have been 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 changes occurs in serum potassium and sodium levels in most patients. Metabolic acidosis occasionally occurs. Electrolyte imbalance may also indicate excessive dosage or to 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 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 to 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, hypertension, gastrointestinal disturbance and muscular weakness may occur. Treatment consists of the induction of vomiting and/or gastric lavage, correction of fluid depletion and electrolyte imbalance, and symptomatic and supportive therapy. If hypertension persists after adequate fluid replacement, dopamine may be used and expert advice sought. Cardiac rhythm should be monitored and appropriate measure to be taken to correct hyperkalaemia as necessary. Renal dialysis may be some benefit in cases of severe overdosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

“Dyazide” contains triamterene and hydrochlorothiazide. Triamterene is a potassium conversing 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, peak hours at two to three hours and tapers off during the subsequent seven to nine hours.

Triamterene is incompletely but fair rapidly absorbed from the gastrointestinal tract. It has been estimated to have 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 gastro-intestinal tract. It is excreted in the urine.

5.3 Preclinical safety data

Recent review of pre-clinical animal studies has suggested that triamterene is carcinogenic in both sexes of mice and in male rats. Such effects have not been reported in human clinical use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch
Povidone 30
Sodium Laurilsulfate
Sunset Yellow (E110)
Sodium Starch Glycollate Type A
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years

6.4 Special precautions for storage

This medicinal product does not require any special special storage conditions.

6.5 Nature and contents of container

Opaque PVC/PVdC/Aluminium foil blister pack containing 30 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Ltd
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85 King William Street
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8 MARKETING AUTHORISATION NUMBER

PA 899/9/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 01 April 2008

10 DATE OF REVISION OF THE TEXT

March 2014