SUMMARY OF PRODUCT CHARACTERISTICS OF BENDURIC 5 MG TABLET

1. Name of the medicinal product

Benduric 5 mg tablet

2. Qualitative and quantitative composition

Each tablet contains 5 mg of Bendroflumethiazide.

3. Pharmaceutical form

Uncoated tablet

4. Clinical particulars

4.1 Therapeutic indications

It is indicated for:

1. Cases where the reduction of fluid retention by diuresis is required; oedema of cardiac, renal or hepatic origin and iatrogenic oedema

2. Bendroflumethiazide produces a moderate but usefully prolonged fall of blood pressure in hypertensive patients. It may be used as the sole antihypertensive agent, or, as an adjunct to other drugs whose action it potentiates. In non-oedematous patients, there may be little noticeable diuretic effect.

4.2 Posology and method of administration

Posology

It is recommended that the tablets should be taken in the morning to avoid nocturia.

Adults and children aged 12 years and over:

Oedema:

Initially 5-10mg once daily or on alternate days.

Maintenance: 2.5-10mg two or three times weekly.

Hypertension: 2.5-5mg once daily. When Bendroflumethiazide is used concurrently with other specific hypotensive agents, the dosage of such agents should be reduced and then adjusted as necessary.

Paediatric population

Children under 12 years: Initial dose of 400micrograms/kg of body weight daily reducing to the maintenance dose of 50-100micrograms/kg daily.

A more appropriate dosage form may be required.

Elderly: Dosage may need to be reduced in the elderly, especially where there is impairment of renal function.

Method of Adminstration

For oral administration.

4.3 Contraindications

• Hypersensitivity to the active substance, to thiazides or to any of the excipients.

• Severe renal or hepatic insufficiency.

• Hypercalcaemia; refractory hypokalaemia; hyponatraemia; symptomatic hyperuricaemia.

• Addison's disease.

4.4 Special warnings and precautions for use

• Bendroflumethiazide may raise serum uric acid levels with consequent exacerbation of gout in susceptible patients.

• Thiazide diuretics should be used with caution in patients with mild or moderate renal or hepatic dysfunction. Renal function should be monitored during bendroflumethiazide therapy. Thiazides can cause electrolyte imbalance which is more severe in patients with hepatic and renal impairment and in those receiving higher or prolonged doses. Elderly patients and those on long term treatment need regular blood tests to monitor electrolyte levels. Hypokalaemia should be corrected by adding potassium supplements to the regimen. The risk of hypomagnesaemia is increased in alcoholic cirrhosis.

• Thiazides may decrease urinary calcium excretion and may cause intermittent and slight elevation of serum calcium. Marked hypercalcaemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function

• Systemic lupus erythematosus (SLE) may be exacerbated by bendroflumethiazide.

• Diabetes Mellitus may be aggravated by bendroflumethiazide.

• Caution is required when treating patients with porphyria.

4.5 Interaction with other medicinal products and other forms of interaction

• *Allopurinol:* Bendroflumethiazide may antagonise the action of allopurinol by causing retention of urate in the kidney. Caution is advised when using this combination.

• *Anion exchange resins:* Colestyramine and colestipol reduce absorption of bendroflumethiazide. This can be prevented by leaving an interval of two hours between doses of bendroflumethiazide and the anion exchange resin.

• *Antiarrhythmics:* The cardiotoxicity of disopyramide, amiodarone, flecainide and quinidine is increased if hypokalaemia occurs following the administration of bendroflumethiazide. The actions of lidocaine and mexiletine are antagonised by hypokalaemia.

• *Antidepressants:* There is an increased risk of postural hypotension if bendroflumethiazide is given with tricyclic antidepressants. There may also be a risk of hypokalaemia if thiazides are given with reboxetine. Concomitant use with MAOIs may result in an enhanced hypotensive effect.

• *Antidiabetics:* Bendroflumethiazide antagonises the hypoglycaemic effects of sulfonylureas, with a potential loss of diabetic control.

• *Antiepileptics:* There is an increased risk of hyponatraemia when bendroflumethiazide and carbamazepine are take concurrently.

• *Antifungals:* The risk of hypokalaemia is increased when amphotericin and bendroflumethiazide are taken concurrently.

• *Antihypertensives:* Bendroflumethiazide may enhance the antihypertensive effect of ACE inhibitors and angiotensin-II antagonists. There is an increased risk of first dose hypotension if prazosin is given to a patient taking bendroflumethiazide.

• *Antipsychotics:* Hypokalaemia increases the risk of ventricular arrhythmias with pimozide or thioridazine so concomitant use should be avoided.

4.6 Pregnancy and lactation

Pregnancy

Bendroflumethiazide is best avoided for the management of oedema or hypertension in pregnancy as it crosses the placenta and its use may be associated with hypokalaemia, increased blood viscosity and reduced placental perfusion.

There is insufficient evidence of safety in human pregnancy and foetal bone marrow depression, thrombocytopenia and neonatal jaundice have been described.

Breast-feeding

Bendroflumethiazide suppresses lactation and, although the amounts passing into breast milk are small, it should be avoided in breast feeding mothers.

4.7 Effects on ability to drive and use machines

As bendroflumethiazide can cause dizziness, patients should make sure they are not affected before driving or operating machinery.

4.8 Undesirable effects

Blood and the lymphatic system disorders Rare	blood dyscrasias, including agranulocytosis, aplastic anaemia, thrombocytopenia and leucopenia
Immune system disorders not known	Rashes (including exfoliative dermatitis), photosensitivity, pneumonitis and pulmonary oedema have been reported occasionally.
Metabolism and nutrition disorders not known	Bendroflumethiazide may lower carbohydrate tolerance and the insulin dosage of some diabetic patients may require adjustment. Care is required when bendroflumethiazide is administered to patients with a known predisposition to diabetes. Bendroflumethiazide may raise serum uric acid levels and exacerbate gout in susceptible individuals. Plasma lipids may be altered in patients taking bendroflumethiazide. Bendroflumethiazide administration may cause hypokalaemia, hypomangnesaemia, hyponatraemia,

	hypercalcaemia and hypochloraemic alkalosis. Hypokalaemia may result in polyuria, malaise, muscle weakness or cramp, dizziness, nausea, anorexia or vomiting.

4.9 Overdose

Symptoms: Nausea, vomiting, diarrhoea, dehydration, dizziness, weakness, muscle cramps, diuresis, increased frequency of micturition with polyuria and thirst. Extreme cases may show depletion of intravascular volume, hypotension and peripheral circulatory failure. Hypokalaemia and mild hypoglycaemia are likely to be present if diuresis is profound. CNS depression (*eg* drowsiness, lethargy and coma) may occur without cardiovascular or respiratory depression.

Treatment: Activated charcoal may help reduce absorption of substantial amounts if given within one hour of ingestion. Treatment should be symptomatic and directed at fluid and electrolyte replacement which should be monitored together with the blood pressure and renal function. Hyponatraemia should be treated with water deprivation rather than by the administration of sodium chloride. Cathartics should be avoided.

5. Pharmacological properties

5.1 Pharmacodynamic properties

The mechanism whereby the thiazides exert their antihypertensive effect has not been clearly established.

Bendroflumethiazide inhibits the renal tubular absorption of salt and water by its action at the beginning of the distal convoluted tubule. Sodium and chloride ions are excreted in equivalent proportions. Because potassium excretion is promoted, metabolic alkalosis may occur secondary to hypokalaemia. There is no important effect upon carbonic anhydrase. Bendroflumethiazide exerts its diuretic effect in about 2 hours and this lasts for 12 to 18 hours or longer.

5.2 Pharmacokinetic properties

Absorption:

Bendroflumethiazide has been reported to be completely absorbed from the gastrointestinal tract. Diuresis is initiated in about 2 hours and lasts for 12-18 hours or longer.

Distribution:

Bendroflumethiazide is more than 90% bound to plasma proteins.

Biotransformation:

There are indications that it is fairly extensively metabolised. Peak plasma levels are reached in 2 hours and a plasma half- life of between 3 and 8.5 hours on average.

Elimination:

About 30% is excreted unchanged in the urine with the remainder excreted as uncharacterized metabolites.

5.3 Preclinical safety data

Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose BP

Magnesium stearate BP

Aerosil BP

Potassium sorbate BP

Maize starch BP

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C in a dry place in the absence of light.

6.5 Nature and contents of container

PVC/Aluminium foil, Packs of 28 Tablets in a carton

6.6 Special precautions for disposal and other handling

Not applicable.

7 Registrant

Cosmos Limited

8 Manufacturer

Cosmos Limited

Rangwe Road; Off Lunga Lunga, Industrial Area

P.O Box 41433, GPO 00100-Nairobi

Kenya

Telephone: + (254-20) 2519603/4/5, 020 8042200/2/3/4/5

Telefax: +254-020-8096280/1

E-mail: admin@cosmos-pharm.com