SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Bumetanide 1 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1 mg of bumetanide

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet
White, circular, flat uncoated tablet. Engraving: 7B1: plain with breakline.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Bumetanide is indicated when diuretic therapy is required in the treatment of oedema, such as that associated with congestive heart failure, cirrhosis of the liver and renal disease including nephrotic syndrome. Bumetanide 1 mg tablets are indicated in the treatment of oedema, and treatment of arterial hypertension in adults. Bumetanide 5 mg tablets are indicated in the treatment of acute and chronic renal failure in adults and may be used in oedema of cardiac or renal origin where high doses of a potent short acting diuretic are required.

4.2 Posology and method of administration

For oral administration.

Adults
Normally a single dose of 1 mg given in the morning or early evening. A second dose can be given 6 to 8 hours later depending on patient response.

In refractory oedema higher doses may be necessary, until a satisfactory diuretic response is obtained.

Paediatric population
The medicinal product is not recommended for children as there is limited information on safety, efficacy and dosage in children.

Elderly
Dosage should be adjusted according to response. A dose of 0.5 mg per day may be sufficient in some elderly patients.

4.3 Contraindications

Hypersensitivity to bumetanide or to any of the excipients listed in section 6.1.

Bumetanide can be used to induce diuresis in renal insufficiency. Therapy should be stopped if there is significant increase in blood urea levels or the onset of oliguria or anuria is observed during the treatment of severe renal disease.

Bumetanide is contra-indicated in hepatic coma, care should be taken in cases of severe electrolyte imbalance.

4.4 Special warnings and precautions for use

Very rapid mobilisation of oedema, particularly in the elderly, may cause sudden changes in cardiovascular pressure-flow relationships with circulatory collapse and should be borne in mind when bumetanide is given in high doses intravenously or orally.

Electrolyte disturbances may occur particularly in those patients taking a low-salt diet. Periodic checks of serum electrolyte levels, in particular sodium, potassium, chlorides and bicarbonates should be undertaken and where necessary replacement therapy instituted.

As with other diuretics, bumetanide may cause an increase in blood uric acid. Regular checks on urine and blood glucose should be made in diabetics and patients suspected of latent diabetes.

Patients with chronic renal failure on high doses of bumetanide should remain under constant hospital supervision.

Encephalopathy may be precipitated in patients with pre-existing hepatic impairment.

Toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS), which can be life-threatening or fatal, have been reported in relation to non-antibiotic sulphonamide containing products, including bumetanide. Patients should be advised of the signs and symptoms of SJS and TEN and closely monitored for those. If signs and symptoms suggestive of these reactions appear, bumetanide should be withdrawn, and an alternative therapy should be considered. If the patient has developed a serious reaction such as SJS or TEN, with the use of bumetanide, treatment with bumetanide must not be restarted in this patient at any time.

Excipient(s)
Lactose
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Like other diuretics, bumetanide shows a tendency to increase potassium excretion which can lead to an increase in the sensitivity of the myocardium to the toxic effects of digitalis. Therefore, the dose of bumetanide may need adjustment when given in conjunction with cardiac glycosides.

Bumetanide may potentiate the effects of antihypertensive drugs. Therefore, patients taking these drugs should be monitored and dosage adjustment should occur where necessary.

Certain non-steroidal anti-inflammatory drugs have been shown to antagonise the action of diuretics.

Bumetanide should be used with caution in patients already receiving nephrotoxic or ototoxic drugs.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with bumetanide. This may result in increased lithium toxicity, including increased risk of cardiotoxic and neurotoxic effects of lithium. Therefore, it is recommended that lithium levels are carefully monitored and where necessary the lithium dosage is adjusted in patients receiving this combination.

4.6 Fertility, pregnancy and lactation

Avoid the use of bumetanide in the first trimester of pregnancy.

It is unknown whether bumetanide can be excreted into breast milk, therefore, its use during lactation is not recommended. If the drug is absolutely necessary for the mother, nursing mothers should either stop breast feeding or observe the infant for any adverse effects.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Reported reactions include abdominal pain, vomiting, dyspepsia, diarrhoea, stomach and muscle cramps, arthralgia, fatigue, hypotension, headache, dizziness, nausea, encephalopathy in patients with pre-existing hepatic disease, fluid and electrolyte

depletion, dehydration, hyperuricaemia, raised blood urea and serum creatinine, hyperglycaemia, abnormalities of serum levels of hepatic enzymes, skin rashes, pruritus, urticaria, thrombocytopenia, gynaecomastia and painful breasts.

Bone marrow depression associated with the use of bumetanide has been reported rarely but it has not been definitely proven to be attributed to the drug.

Hearing disturbance after administration of bumetanide is rare and reversible.

High dose therapy - In patients with severe chronic renal failure given high doses of bumetanide, there have been reports of severe generalised, muscoskeletal pain sometimes associated with muscle spasm, occurring 1 to 2 hours after administration and lasting up to 12 hours. The lowest reported dose causing this type of adverse reaction was 5 mg by intravenous injection and the highest dose was 75 mg orally in a single dose. All patients recovered fully and there was no deterioration in their renal function. The cause of this pain is uncertain but it may be as a result of varying electrolyte gradients at the cell membrane level. Experience suggests that the incidence of such reactions is decreased by initiating treatment at 5 - 10 mg daily and titrating upwards using a twice daily dosage regimen at doses of 20 mg per day or more.

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), have been reported in association with bumetanide (see section 4.4), the frequency of this is not known.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professional are asked to report any suspected adverse reactions via the Yellow Card Scheme website at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

Symptoms are those caused by excessive diuresis. The stomach should be emptied by gastric lavage or emesis. General measures should be taken to restore blood volume, maintain blood pressure and correct electrolyte disturbance.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: C03C A02 (sulfonamides, plain)

Bumetanide is a potent high ceiling loop diuretic with a rapid onset and short duration of action. The primary site of action is the ascending limb of the loop of Henlé. It exerts inhibitory effects on electrolyte reabsorption causing the diuretic and natriuretic action observed.

After oral administration of 1mg of bumetanide, diuresis begins within 30 minutes with a peak effect between one and two hours. The diuretic effect is virtually complete in three hours after a 1mg dose.

5.2 Pharmacokinetic properties

Bumetanide is well absorbed after oral administration with bioavailability reaching between 80 and 95%. The elimination half-life ranges from between 0.75 to 2.6 hours. No active metabolites are known. Renal excretion accounts for approximately half the clearance with hepatic excretion responsible for the other half. There is an increase in half-life and a reduced plasma clearance in the presence of renal or hepatic disease. In patients with chronic renal failure, the liver takes more importance as an excretory pathway although the duration of action is not markedly prolonged.

In neonates and infants, elimination appears slower than in older paediatric patients and adults, possibly because of immature renal and hepatobiliary functions. Mean serum elimination half-life decreases during the first month of life from 6 hours in neonates to 2.4 hours in infants 1 month of age.
Mean serum elimination half-life is 2.5 and 1.5 hours in infants younger than 2 months of age and in those 2–6 months of age, respectively. The apparent elimination half-life may be prolonged to approximately 6 hours (with a range up to 15 hours) after IV administration in premature or full-term neonates with respiratory disorders. Data for younger children, including neonates and infants, is not sufficient to allow for dosing recommendations, see 4.2.

5.3 Preclinical safety data

Preclinical information has not been included because the safety profile of bumetanide has been established after many years of clinical use. Please refer to Section 4.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Microcrystalline cellulose (E460)
Maize starch
Povidone (E1201)
Sodium starch glycollate (Type A) (E576)
Magnesium stearate (E572)

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

18 months.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container.

6.5 Nature and contents of container

HDPE containers with LDPE lids in packs of 14, 20, 21, 28, 30, 50, 56, 60, 84, 100, 112, 120, 168, 250, 500, 1000 & 5000.

PVdC coated PVC film with hard temper aluminium foil blister strips in packs of 7, 10, 14, 20, 21, 28, 30, 50, 56, 60, 84, 90, 100, 110, 112, 120, 150, 160 & 168

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited,
Ridings Point,
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WF10 5HX,
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8. MARKETING AUTHORISATION NUMBER

PL 00289/0322

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/08/2003

10 DATE OF REVISION OF THE TEXT

14/11/2024