1 SUMMARY OF PRODUCT CHARACTERISTICS

2 NAME OF THE MEDICINAL PRODUCT

Bumetanide 0.2 mg/ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 0.2 mg bumetanide.

Excipient(s) with known effect
Each ml of this medicine contains 275 mg sorbitol, 1.5 mg methyl parahydroxybenzoate and 0.15 mg propyl parahydroxybenzoate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.
Bumetanide oral solution is a clear, green liquid with the flavour of peppermint.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Bumetanide is indicated whenever diuretic therapy is required in the treatment of oedema, e.g. that associated with congestive heart failure, cirrhosis of the liver and renal disease including the nephrotic syndrome.

4.2 Posology and method of administration

Posology

Adults, adolescents and children aged 12 years and older
Usually 1 mg (5 ml) as a single oral dose given morning or early evening. The dosage should be adjusted according to the patient's response.

Elderly
Adjust dosage according to response: a dose of 0.5 mg bumetanide per day may be
sufficient in some elderly patients.

Paediatric population (children under 12 years)
Bumetanide Liquid should not be used for children under 12 years of age.

Method of administration
For oral administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listen in section 6.1.

Although bumetanide can be used to induce diuresis in renal insufficiency, any marked increase in blood urea or the development of oliguria or anuria during treatment of severe progressing renal disease are indications for stopping treatment with bumetanide.

Bumetanide is contra-indicated in hepatic coma and care should be taken in states of severe electrolyte depletion.

4.4 Special warnings and precautions for use

Excessively rapid mobilisation of oedema particularly in elderly patients may give rise to sudden changes in cardiovascular pressure flow relationships with circulatory collapse. This should be borne in mind when bumetanide is given in high doses. Electrolyte disturbances may occur, particularly in those patients taking a low salt diet. Regular checks of serum electrolytes, in particular sodium, potassium, chloride and bicarbonate should be performed, and replacement therapy instituted where indicated.

As with other diuretics, bumetanide may cause an increase in blood uric acid. Periodic checks on urine and blood glucose should be made in diabetics and patients suspected of latent diabetes (see section 4.5).

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

Caution is advised when used in patients with hypotension and in patients with porphyria.

Caution should be exercised when used in patients with hepatic impairment as there may be increased risk of encephalopathy.

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

In patients with known hypersensitivity to sulfonamides or thiazides there may be a potential risk of hypersensitivity to bumetanide.

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.

Bumetanide found in urine by doping test is cause for disqualification of athletes.

Excipients:

This medicine contains 1375 mg sorbitol in each spoonful (5 ml) which is equivalent to 275 mg/ml. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

This medicine contains methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reaction (possibly delayed).

This medicine contains less than 1 mmol sodium (23 mg) per spoonful (5 ml), that is to say essentially ‘sodium-free’

4.5 Interaction with other medicinal products and other forms of interaction

In common with other diuretics, serum lithium levels may be increased when lithium is given concurrently 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.
Like other diuretics, bumetanide shows a tendency to increase the excretion of potassium which can lead to an increase in the sensitivity of the myocardium to the toxic effects of digitalis. Thus the dose may need adjustment when given in conjunction with cardiac glycosides.
Bumetanide may potentiate the effects of antihypertensive drugs. Therefore, the dose of the latter may need adjustment when bumetanide is used to treat oedema in hypertensive patients.
Certain non-steroidal anti-inflammatory drugs have been shown to antagonise the action of diuretics.

4.6 Fertility, Pregnancy and lactation

Pregnancy
There are no adequate data from the use of Bumetanide Liquid in pregnant women. Bumetanide should not be used during pregnancy unless clearly necessary. It may be used only when the potential benefit justifies the potential risk to the foetus.

Breast-feeding
There is insufficient information on the excretion of Bumetanide in human or animal breast milk. Therefore, Bumetanide should not be taken by nursing mothers.

4.7 Effects on ability to drive and use machines

Patients who experience dizziness or fatigue should not drive or operate machinery.

8.8 Undesirable effects

The following side effects, listed below by system organ class, have been reported to be associated with bumetanide use. Since only post marketing data are available, the frequency for these side effects is unknown.

Blood and lymphatic system disorders
Thrombocytopenia, leukopenia, bone marrow failure, agranulocytosis

Immune system disorders
Hypersensitivity

Metabolism and nutrition disorders
Electrolyte imbalance, for example:
Hypokalaemia, hyponatraemia, dehydration, hypomagnesaemia, gout, hyperuricaemia, alkalosis hypochloraemic, hyperglycaemia, hypocalcaemia, hyperlipidaemia

Nervous system disorders
Headache, dizziness

Ear and labyrinth disorders
Tinnitus, deafness

Vascular disorders
Orthostatic hypotension, hypotension

Gastrointestinal disorders
Gastrointestinal disorder, for example:
Nausea, vomiting, diarrhoea, abdominal pain

Hepatobiliary system disorders
Cholestasis, jaundice

Skin and subcutaneous tissue disorders
Rash*, urticaria, dermatitis, photosensitivity reaction, pruritus, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN).

*Various types of rash reactions such as erythematous, maculo-papular and pustular have been reported.

Musculoskeletal, connective tissue and bone disorders
Myalgia, muscle spasm, arthralgia

Renal and urinary disorders
Renal failure acute

Reproductive system and breast disorders
Gynaecomastia, breast pain

General disorders and administrative site conditions
Fatigue

Investigations
Blood creatinine increased

High Dose Therapy
In patients with severe chronic renal failure given high doses of bumetanide, there have been reports of severe, generalised, musculoskeletal pain sometimes associated with muscle spasm, occurring one or two 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 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 a result of varying electrolyte gradients at the cell membrane level.

Experience suggests that the incidence of such reactions is reduced 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.

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 professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms would be those caused by excessive diuresis. Empty stomach 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

Pharmacotherapeutic group: High-ceiling diuretics. Sulfonamides, plain
ATC code: C03CA02
Bumetanide is a potent, high ceiling diuretic with a rapid onset and a short duration of action.

5.2 Pharmacokinetic properties

After oral administration of 1 mg 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 1 mg dose.

In most patients 1 mg of bumetanide produces a similar diuretic effect to 40 mg of furosemide.

Bumetanide is well absorbed after oral administration. Bumetanide excretion in the urine shows a good correlation with the diuretic response. In patients

with chronic renal failure, the liver takes more importance as an excretory pathway, although the duration of action in such patients is not markedly prolonged.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl-para-hydroxybenzoate (E 218)
Propyl-para-hydroxybenzoate (E 216)
Sorbitol (E 420)
Xanthan gum
Sodium citrate
Patent blue V
Quinoline yellow
Peppermint flavour
Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Amber glass bottles with plastic screw caps, of 5, 10, 25 and 150 ml.

Not all pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Rosemont Pharmaceuticals Ltd
Rosemont House
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Braithwaite Street
Leeds
LS11 9XE
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00427/0281

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