SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Furosemide Tablets 20mg.
Furosemide Tablets 40mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Furosemide Tablets 20 mg: Each tablet contains 20mg of Furosemide
Furosemide Tablets 40 mg: Each tablet contains 40mg of Furosemide

Excipient with known effect:
Furosemide Tablets 20 mg: Each tablet contains 52.5 mg lactose.
Furosemide Tablets 20 mg: Each tablet contains 105 mg lactose.

For the full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, flat bevelled edge tablets engraved with company logo on one side and a breakline and A270 on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Furosemide is a diuretic recommended for use in all indications where a prompt and effective diuresis is required.

1) The treatment of oedema associated with congestive heart failure, cirrhosis of the liver, renal disease including nephrotic syndrome and pulmonary oedema.

2) The treatment of peripheral oedema due to mechanical obstruction, venous insufficiency, mild to moderate hypertension.

4.2 Posology and method of administration

Posology

Furosemide has a very wide therapeutic range, the effect being proportional to dosage.
Furosemide is best given as a single dose either daily or on alternate days.

Adults and children over 12 years:
Oedema: Initially 40mg daily in the morning; ordinarily a prompt diuresis ensues and the starting dose can then be maintained or even reduced. Diuresis lasts for approximately four hours following administration and hence the time of administration can be adjusted to suit the patient's requirements. Maintenance dose is 20mg daily or 40mg on alternate days, increased in resistant oedema to 80mg daily.

Hypertension: 20-40mg twice daily; if 40mg twice daily does not lead to a clinically satisfactory response, the addition of other antihypertensive agents, rather than an increase in the dose of furosemide should be considered.

Children under 12 years:
1-3 mg/kg body weight daily. A more suitable dosage form should be used in this age group

Elderly:
In the elderly, furosemide is generally eliminated more slowly. Dosage should be titrated until the required response is achieved (see section 4.4).

Method of administration: Oral

4.3 Contraindications

Known hypersensitivity to furosemide, amiloride or to any of the excipients listed in section 6.1.

Known hypersensitivity to sulphonamides and sulphonamide derivatives.

Anuria or renal failure with anuria not responding to furosemide.

Comatose or pre-comatose states associated with liver cirrhosis (see section 4.4);

Digitalis intoxication (see section 4.5).

Renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents.

Renal failure associated with hepatic coma.

Hypovolaemia and dehydration (with or without accompanying hypotension) (see section 4.4)

Severe hypokalaemia: severe hyponatraemia (see section 4.4).

Impaired renal function with a creatinine clearance below 30ml/min per 1.73 m^2 body surface area (see section 4.4).

Addison's disease (see section 4.4).

Porphyria.

Concomitant potassium supplements or potassium sparing diuretics (see section 4.5).

Breast-feeding women (see section 4.6).

4.4 Special warnings and precautions for use

Conditions requiring correction before furosemide is started (see also section 4.3):

- Hypotension and hypovolaemia
- Severe electrolyte disturbances - particularly hypokalaemia, hyponatraemia and acid-base disturbances.

Furosemide is not recommended:

- In patients at high risk for radiocontrast nephropathy - it should not be used for diuresis as part of the preventative measures against radiocontrast-induced nephropathy.
- In patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Particular caution and/or dose reduction required:

- elderly patients (lower initial dose as particularly susceptible to side-effects - see section 4.2).
- difficulty of micturition including prostatic hypertrophy (increased risk of urinary retention: consider lower dose.
- closely monitor patients with partial occlusion of the urinary tract.
- diabetes mellitus (latent diabetes may become overt: insulin requirements in established diabetes may increase: stop furosemide before a glucose tolerance test).
- pregnancy (see section 4.6).
- gout (furosemide may raise uric acid/precipitate gout)
- patients with hepatorenal syndrome
- impaired hepatic function (see section 4.3 and below - monitoring required).
- impaired renal function (see section 4.3 and below - monitoring required).
- adrenal disease (see section 4.3 - contraindication in Addison's disease).
- hypoproteinaemia e.g. nephrotic syndrome (effect of furosemide may be impaired and its ototoxicity potentiated - cautious dose titration required).

- acute hypercalcaemia (dehydration results from vomiting and diuresis - correct before giving furosemide). Treatment of hypercalcaemia with a high dose of furosemide results in fluid and electrolyte depletion - meticulous fluid replacement and correction of electrolyte required.
- patients who are at risk from a pronounced fall in blood pressure
- premature infants (possible development nephrocalcinosis/nephrolithiasis; renal function must be monitored and renal ultrasonography performed)
- Symptomatic hypotension leading to dizziness, fainting or loss of consciousness can occur in patients treated with furosemide, particularly in the elderly, patients on other medications which can cause hypotension and patients with other medical conditions that are risks for hypotension.

Avoidance with other medicines (see also section 4.5 for other interactions):
- concurrent NSAIDs should be avoided - if not possible diuretic effect of furosemide may be attenuated.
- ACE-inhibitors & Angiotensin II receptor antagonists - severe hypotension may occur - dose of furosemide should be reduced/stopped (3 days) before starting or increasing the dose of these.

Laboratory monitoring requirements:
- Serum sodium
  Particularly in the elderly or in patients liable to electrolyte deficiency.
- Serum potassium

The possibility of hypokalaemia should be taken into account, in particular in patients with cirrhosis of the liver, those receiving concomitant treatment with corticosteroids, those with an unbalanced diet and those who abuse laxatives. Regular monitoring of plasma electrolytes, particularly sodium and potassium should be carried out and electrolyte replacement therapy instituted accordingly, and if necessary treatment with a potassium supplement, is recommended in all cases, but is essential at higher doses and in patients with impaired renal function. It is especially important in the event of concomitant treatment with digoxin, as potassium deficiency can trigger or exacerbate the symptoms of digitalis intoxication (see section 4.5). During long-term or high dose therapy potassium supplements are recommended.

Frequent checks of the serum potassium are necessary in patients with impaired renal function and creatinine clearance below 60ml/min per 1.73m2 body surface area as well as in cases where furosemide is taken in combination with certain other drugs which may lead to an increase in potassium levels (see section 4.5 & refer to section 4.8 for details of electrolyte and metabolic abnormalities).

- Renal function

Marked diuresis can cause reversible impairment of kidney function in patients with renal dysfunction. Frequent BUN determinations during the first few months of treatment, periodically thereafter. Long-term/high-dose BUN should regularly be measured. Adequate fluid intake is necessary in such patients. Serum creatinine and urea levels tend to rise during treatment.

- Glucose

Adverse effect on carbohydrate metabolism - exacerbation of existing carbohydrate intolerance or diabetes mellitus. Regular monitoring of blood glucose levels is desirable.

- Other electrolytes

Patients with hepatic failure/alcoholic cirrhosis are particularly at risk of hypomagnesia (as well as hypokalaemia). During long-term therapy (especially at high doses) magnesium, calcium, chloride, bicarbonate and uric acid should be regularly measured.

Clinical monitoring requirements (see also section 4.8):

Regular monitoring for

- blood dyscrasias (If these occur, stop Furosemide immediately)
- liver damage
- idiosyncratic reactions.

Other alterations in lab values:

Serum cholesterol and triglyceride levels may rise during furosemide treatment but will usually return to normal within six months of starting furosemide

Concomitant use with risperidone

In risperidone placebo-controlled trials in elderly patients with dementia, a higher incidence of mortality was observed in patients treated with furosemide plus risperidone (7.3%; mean age 89 years, range 75-97 years) when compared to patients treated with risperidone alone (3.1%; mean age 84 years, range 70-96 years) or furosemide alone (4.1%; mean age 80 years, range 67-90 years). Concomitant use of risperidone with other diuretics (mainly thiazide diuretics used in low dose) was not associated with similar findings.

No pathophysiological mechanism has been identified to explain this finding, and no consistent pattern for cause of death observed. Nevertheless, caution should be exercised and the risks and benefits of this combination or co-treatment with other potent diuretics should be considered prior to the decision to use. There was no increased incidence of mortality among patients taking other diuretics as concomitant treatment with risperidone. Irrespective of treatment, dehydration was an overall risk factor for mortality and should therefore be avoided in elderly patients with dementia (see section 4.3 Contraindications).

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

General: The dosage of concurrently administered cardiac glycosides, diuretics, anti-hypertensive agents, or other drug with blood-pressure-lowering potential may require adjustment as a more pronounced fall in blood pressure must be anticipated if given concomitantly with furosemide.

The toxic effects of nephrotoxic drugs may be increased by concomitant administration of potent diuretics such as furosemide.

Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain other drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).

Antihypertensives: enhanced hypotensive effect possible with all types. Concurrent use with ACE Inhibitors or Angiotensin-II receptor antagonists can result in marked falls in blood pressure furosemide should be stopped or the dose reduced before starting an ACE inhibitor or Angiotensin II receptor antagonists (see section 4.4).

Alcohol: enhanced hypotensive effect

Aminoglutethimide: Concomitant administration may increase the risk of hyponatraemia.

Antifungals: increased risk of hypokalaemia and nephrotoxicity with amphotericin.

NSAIDs: increased risk of nephrotoxicity of NSAIDs. Indometacin and ketorolac may antagonise the effects of furosemide (avoid if possible; see section 4.4).

Salicylates: Effects may be potentiated by furosemide. Salicylic toxicity may be increased by furosemide.

Anti-arrhythmics: (including amiodarone, disopyramide, flecainide and Sotalol) -risk of cardiac toxicity (because of furosemide-induced hypokalaemia). The effects of lidocaine, tocainide or mexiletine may be antagonised by furosemide.

Antibiotics: increased risk of ototoxicity with aminoglycosides, polymixins or vancomycin - only use concurrently if compelling reasons. Increased risk of nephrotoxicity of with cefaloridine or aminoglycosides. Furosemide can decrease vancomycin serum levels after cardiac surgery. Increased risk of hyponatraemia with trimethoprim. Impairment of renal function may develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins.

Antidepressants: enhanced hypotensive effect with MAOIs. Increased risk of postural hypotension with TCAs (tricyclic antidepressants). Increased risk of hypokalaemia with reboxetine.

Antidiabetics: hypoglycaemic effects antagonised by furosemide.

Anaesthetics: enhanced hypotensive effect when diuretics are given with general anaesthetics. The effects of curare may be enhanced by furosemide.

Antiepileptics: increased risk of hyponatraemia with carbamazepine. Diuretic effect reduced by phenytoin.

Antihistamines: hypokalaemia with increased risk of cardiac toxicity.

Anxiolytics and hypnotics: enhanced hypotensive effect. Chloral or triclofos may displace thyroid hormone from binding site.

CNS stimulants (drugs used for ADHD) - hypokalaemia increases the risk of ventricular arrhythmias.

Antipsychotics: Furosemide induced hypokalaemia increases the risk of cardiac toxicity. Avoid concurrent use with pimozide. Increased risk of ventricular arrhythmias with amisulpride or sertindole. Enhanced hypotensive effect with phenothiazines.

When administering risperidone, caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide or with other potent diuretics should be considered prior to the decision to use. See section 4.4 Special warnings and precautions for use regarding increased mortality in elderly patients with dementia concomitantly receiving risperidone.

Cardiac glycosides: hypokalaemia and electrolyte disturbances (including hypomagnesia) increase the risk of cardiac toxicity.

Drugs that prolong Q-T interval: increased risk of toxicity with furosemide-induced electrolyte disturbances.

Renin inhibitors: aliskiren reduces plasma concentrations of furosemide given orally. Reduced effect of furosemide might be observed in patients treated with both aliskiren and oral furosemide, and it is recommended to monitor for reduced diuretic effect and adjust the dose accordingly.

Nitrates: enhanced hypotensive effect.

Corticosteroids: increased risk of hypokalaemia. Antagonism of diuretic effect (sodium retention).

Glychyrrizin (contained in liquorice): may increase the risk of developing hypokalaemia.

Cytotoxics: increased risk of nephrotoxicity and ototoxicity with platinum compounds/ cisplatin. Nephrotoxicity of cisplatin may be enhanced if furosemide is not given in low doses (e.g. 40 mg in patients with normal renal function) and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.

Anti-metabolites: effects of furosemide may be reduced by methotrexate and furosemide may reduce renal clearance of methotrexate.

Dopaminergics: enhanced hypotensive effect with levodopa.

Immunomodulators: enhanced hypotensive effect with aldesleukin. Increased risk of hyperkalaemia with ciclosporin and tacrolimus. Increased risk of gouty arthritis with ciclosporin.

Other diuretics: profound diuresis possible if metolazone given with furosemide. Increased risk of hyperkalaemia (see section 4.3).

Lithium: In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with furosemide, resulting in 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.

Chelating agents: sucralfate may decrease the gastro-intestinal absorption of furosemide - the 2 drugs should be taken at least 2 hours apart.

Vasodilators: Moxisylyte (Thymoxamine) or hydralazine: enhanced hypotensive effect.

Muscle Relaxants: enhanced hypotensive effect with baclofen and tizanidine. Increased effect of curare like muscle relaxants.

Oestrogens: diuretic effect antagonized.

Progestogens: (drospirenone) increased risk of hyperkalaemia.

Prostaglandins: enhanced hypotensive effect with alprostadil.

Sympathomimetics: increased risk of hypokalaemia with high doses of $beta_2$ sympathomimetics.

Probenecid: effects of furosemide may be reduced by probenecid and furosemide may reduce renal clearance of probenecid.

Theophylline: Enhanced hypotensive effect.

Carbenoxolone: May increase the risk of developing hypokalaemia.

Laxative abuse: Increases the risk of potassium loss.

Others: Concomitant administration of aminoglutethimide may increase the risk of hyponatraemia.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is clinical evidence of safety of the drug in the third trimester of human pregnancy and furosemide has been given after the first trimester of pregnancy for oedema, hypertension and toxaemia of pregnancy without causing fetal or newborn adverse effects furosemide. However, furosemide crosses the placental barrier and should not be given during pregnancy unless there are compelling medical reasons. It should only be used for the pathological causes of oedema which are not directly or indirectly linked to the pregnancy. The treatment with diuretics of oedema and hypertension caused by pregnancy is undesirable because placental perfusion can be reduced, so, if used, monitoring of fetal growth is required.

Breast-feeding (see section 4.3)
Furosemide is contraindicated as it may pass into breast milk and inhibit lactation.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Reduced mental alertness, dizziness and blurred vision have been reported, particularly at the start of treatment, with dose changes and in combination with alcohol. Patients should be advised that if affected, they should not drive, operate machinery or take part in activities where these effects could put themselves or others at risk.

4.8 Undesirable effects

Undesirable effects can occur with the following frequencies: very common (> 1/10), common (> 1/100, < 1/10), uncommon (> 1/1,000, < 1/100), rare (> 1/10,000, < 1/1,000) and very rare (< 1/10,000, including isolated reports).

Blood and lymphatic system disorders:
Uncommon: Thrombocytopenia

Rare:

- eosinophilia
- leukopenia
- bone marrow depression (necessitates withdrawal of treatment). The haemopoietic status should therefore be regularly monitored.

Very Rare:

- aplastic anaemia or haemolytic anaemia
- agranulocytosis

Nervous system disorders
Rare:

- paraesthesia
- hyperosmolar coma

Not known:
dizziness, fainting or loss of consciousness caused by symptomatic hypotension.

Endocrine disorder
Glucose tolerance may decrease with furosemide. In patients with diabetes mellitus this may lead to a deterioration of metabolic control; latent diabetes mellitus may become manifest. Insulin requirements of diabetic patients may increase.

Eye disorders
Uncommon: visual disturbance

Ear and labyrinth disorders
Uncommon: deafness (sometimes irreversible)

Hearing disorders, tinnitus, although usually transitory, may occur in rare cases, particularly in patients with renal failure, hypoproteinaemia (e.g. in nephritic syndrome) and/or when intravenous furosemide has been given too rapidly.

Cardiac disorders
Uncommon: cardiac arrhythmias

Furosemide may cause a reduction in blood pressure which, if pronounced may cause signs and symptoms such as impairment of concentration and reactions, light headedness, sensations of pressure in the head, headache, dizziness, drowsiness, weakness, disorders of vision, dry mouth, orthostatic intolerance.

Hepatobiliary disorders
In isolated cases, intrahepatic cholestasis, an increase in liver transaminases or acute pancreatitis may develop.

Hepatic encephalopathy in patients with hepatocellular insufficiency may occur (see Section 4.3).

Vascular Disorder:
Rare: vasculitis

Skin and subcutaneous tissue disorders:
Uncommon: Photosensitivity

Rare: Skin and mucous membrane reactions may occasionally occur, e.g. itching, urticaria, other rashes or bullous lesions, fever, hypersensitivity to light, exudative erythema multiforme (Lyell's syndrome and Stevens-Johnson syndrome), bullous exanthema, various forms of dermatitis (including exfoliative dermatitis), purpura and DRESS (Drug rash with eosinophilia and systemic symptoms).

Not known: AGEP (acute generalized exanthematous pustulosis).

When these occur, treatment with furosemide should be stopped.

Metabolism and nutrition disorders:
As with other diuretics, electrolytes and water balance may be disturbed as a result of diuresis after prolonged therapy. Furosemide leads to increased excretion of sodium and chloride and consequently increased excretion of water. In addition, excretion of other electrolytes (in particular potassium, calcium and magnesium) is increased.

Metabolic acidosis can also occur. The risk of this abnormality increases at higher dosages and is influenced by the underlying disorder (e.g. cirrhosis of the liver, heart failure), concomitant medication (see section 4.5) and diet.

Symptomatic electrolyte disturbances and metabolic alkalosis may develop in the form of a gradually increasing electrolyte deficit or e.g. where higher furosemide doses are administered to patients with normal renal function, acute severe electrolyte losses.

Symptoms of electrolyte imbalance depend on the type of disturbance:

Sodium deficiency can occur; this can manifest itself in the form of confusion, muscle cramps, muscle weakness, loss of appetite, dizziness, drowsiness and vomiting.

Potassium deficiency manifests itself in neuromuscular symptoms (muscular weakness, paralysis), intestinal symptoms (vomiting, constipation, meterorism), renal symptoms (polyuria) or cardiac symptoms. Severe potassium depletion can result in paralytic ileus or confusion, which can result in coma.

Magnesium and calcium deficiency result very rarely in tetany and heart rhythm disturbances.

Serum calcium levels may be reduced; in very rare cases tetany has been observed. Nephrolithiasis/Nephrocalcinosis has been reported in premature infants.

Serum cholesterol (reduction of serum HDL-cholesterol, elevation of serum LDL-cholesterol) and triglyceride levels may rise during furosemide treatment. During long term therapy they will usually return to normal within six months.

As with other diuretics, treatment with Furosemide may lead to transitory increase in blood creatinine and urea levels. Serum levels of uric acid may increase and attacks of gout may occur.

The diuretic action of furosemide may lead to or contribute to hypovolaemia and dehydration, especially in elderly patients. Severe fluid depletion may lead to haemoconcentration with a tendency for thromboses to develop.

General disorders and administration site conditions:
Uncommon: Fatigue

Rare:

- severe anaphylactic or anaphylactoid reactions (e.g. with shock) occur rarely.
- fever
- malaise

Gastrointestinal disorders:
Uncommon: dry mouth, thirst, nausea, bowel motility disturbances, vomiting, diarrhoea, constipation.

Rare: Acute Pancreatitis

The gastro-intestinal disorders such as nausea or gastric upset (vomiting or diarrhoea) and constipation may occur but not usually severe enough to necessitate withdrawal of treatment.

Renal and urinary disorders:
Uncommon: serum creatinine and urea levels can be temporarily elevated during treatment with furosemide.

Rare: interstitial nephritis, acute renal failure.

Increased urine production, urinary incontinence, can be caused or symptoms can be exacerbated in patients with urinary tract obstruction. Acute urine retention, possibly accompanied by complications, can occur for example in patients with bladder disorders, prostatic hyperplasia or narrowing of the urethra.

Pregnancy, puerperium and perinatal conditions
In premature infants with respiratory distress syndrome, administration of Furosemide Tablets in the initial weeks after birth entails an increased risk of a persistent patent ductus arteriosus.

In premature infants, furosemide can be precipitated as nephrocalcinosis/kidney stones.

Rare complications may include minor psychiatric disturbances.

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

Overdosage with furosemide results in dehydration, volume depletion, electrolyte depletion and hypotension and cardiac toxicity due to excessive diuresis. The clinical picture in acute or chronic overdose depends primarily on the extent and consequences of electrolyte and fluid loss, e.g. hypovolaemia, dehydration, haemoconcentration, cardiac arrhythmias due to excessive diuresis. Symptoms of these disturbances include severe hypotension (progressing to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion.High doses have the potential to cause transient deafness and may precipitate gout (disturbed uric acid secretion).

Management
The benefit of gastric decontamination is uncertain. Consider activated charcoal (50g for adults; 1g/kg for children) if an adult or child presents within 1 hour of ingesting a toxic dose.

- Observe for a minimum of 4 hours - monitor pulse and blood pressure.
- Treat hypotension and dehydration with appropriate IV fluids
- Monitor urinary output and serum electrolytes (including chloride and bicarbonate). Correct electrolyte imbalances. Monitor 12 lead ECG in patients with significant electrolyte disturbances

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: High ceiling diuretics sulphonamides, loop diuretics; ATC Code: CO3CA01

The evidence from many experimental studies suggests that furosemide acts along the entire nephron with the exception of the distal exchange site. The main effect is on the ascending limb of the loop of Henley with a complex effect on renal circulation. Blood-flow is diverted from the juxta-medullary region to the outer cortex.

The principle renal action of furosemide is to inhibit active chloride transport in the thick ascending limb. Re-absorption of sodium chloride from the nephron is reduced and a hypotonic or isotonic urine produced.

It has been established that prostaglandin (PG) biosynthesis and the renin-angiotensin system are affected by furosemide administration and that furosemide alters the renal permeability of the glomerulus to serum proteins.

5.2 Pharmacokinetic properties

Approximately 65% of the dose is absorbed after oral administration. The plasma half-life is biphasic with a terminal elimination phase of about 1½ hours. Furosemide is up to 99% bound to plasma proteins and is mainly excreted in the urine, largely unchanged, but also excreted in the bile, non-renal elimination being considerably increased in renal failure. Furosemide crosses the placental barrier and is excreted in milk.

Furosemide is a weak carboxylic acid which exists mainly in the dissociated form in the gastrointestinal tract. Furosemide is rapidly but incompletely absorbed (60-70%) on oral administration and its effect is largely over within 4 hours. The optimal absorption site is the upper duodenum at pH 5.0. Regardless of route of administration 69-97% of activity from a radio-labelled dose is excreted in the first 4 hours after the drug is given. Furosemide is bound to plasma albumin and little biotransformation takes place. Furosemide is mainly eliminated via the kidneys (80-90%); a small fraction of the dose undergoes biliary elimination and 10-15% of the activity can be recovered from the faeces.

In renal/ hepatic impairment:
Where liver disease is present, biliary elimination is reduced up to 50%. Renal impairment has little effect on the elimination rate of furosemide, but less than 20% residual renal function increases the elimination time.

The elderly:
The elimination of furosemide is delayed in the elderly where a certain degree of renal impairment is present.

New born:
A sustained diuretic effect is seen in the newborn, possibly due to immature tubular function.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber that are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose

Pregelatinised maize starch

Sodium starch glycollate

Magnesium stearate

Maize starch

6.2 Incompatibilities

None.

6.3 Shelf life

3 years for opaque plastic containers.

3 years for aluminium/opaque PVC blister packs.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Opaque plastic containers composed of polypropylene tubes and polyethylene tamper-evident closures in pack sizes of 28, 30, 42, 50, 56, 60, 84, 90, 100, 112, 250, 500 and 1,000 tablets.

High density polypropylene or polyethylene containers with tamper-evident or childresistant tamper-evident closures in pack sizes of 28, 30, 42, 50, 56, 60, 84, 90, 100, 112, 250, 500 and 1,000 tablets.

Aluminium/PVC blister packs in pack sizes of 28, 30, 42, 56, 60, 84, 90 and 112 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited
Key House
Sarum Hill
Basingstoke
RG21 8SR
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0079

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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