# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Furosemide 20mg/2ml Solution for Injection.

Furosemide 50mg/5ml Solution for Injection.

Furosemide 250mg/25ml Solution for Injection

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of solution contains 10mg of Furosemide
Excipient(s) with known effect:
Sodium-91.25mg/25ml
For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Colourless or almost colourless sterile solution intended for parenteral administration to human beings.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Furosemide is a potent diuretic and is recommended for use when prompt and effective diuresis is required.

Furosemide Injection 20mg/2ml and 50mg/5ml are appropriate for use in emergencies or where oral therapy is not feasible. The indications include cardiac, pulmonary, hepatic and renal oedema.

Furosemide Injection 250mg/25ml is for use in the management of oliguria due to acute or chronic renal insufficiency with a glomerular filtration rate below 20ml/minute.

## 4.2 Posology and method of administration

Posology

Furosemide Injection 20mg/2ml and 50mg/5ml

*Adults:* Initially, doses of 20 - 50mg may be administered by the intramuscular route, or by slow intravenous injection at a rate not exceeding 4mg/minute. The diuretic effect of furosemide is proportional to the dosage and, if larger doses are required, they should be given as a controlled infusion at a rate not exceeding 4mg/minute and titrated according to the response.

*Elderly:* Elimination of furosemide is generally slower in the elderly. Dosage should be titrated until the required effect is achieved.

*Paediatric population:* Dosages for children range from 0.5 - 1.5mg/kg weight daily up to a maximum total daily dose of 20mg.

Furosemide Injection 250mg/25ml

*Adults:* Furosemide Injection 250mg/25ml is for slow intravenous injection at a rate not exceeding 4mg/minute.

An initial dose of 250mg (one 25ml ampoule) may be added to about 225ml Sodium Chloride Injection B.P. or Ringer's Solution for Injection, and infused over one hour at a drip rate of 80 drops/minute (4mg/minute).

If urine output within the next hour is insufficient, a dose of 500mg (two 25ml ampoules) in an appropriate infusion fluid, the total volume of which must be governed by the patient's state of hydration, may be infused at a rate not exceeding 4mg/minute. If a satisfactory urine output has still not been achieved within one hour following the end of the second infusion, a third dose consisting of 1,000mg (four 25ml ampoules) in an appropriate infusion fluid may be given. The rate of infusion should never exceed 4mg/minute.

If the third infusion (1,000mg over 4 hours) is not effective, dialysis will probably be required.

In oliguric or anuric patients with significant fluid overload, it may not be practicable to use the aforementioned method of administration. In such cases, the use of a constant-rate infusion pump with a micrometer screw-gauge adjustment may be considered for direct administration of the injection into the vein. The rate of infusion should still never exceed 4mg/min.

If the response to either method of administration is satisfactory (urine output 40 - 50ml/hour), the effective dose (of up to 1,000mg) may be repeated every 24 hours. Alternatively, treatment may be maintained by oral administration of Furosemide Tablets, using 500mg by mouth for each 250mg required by injection. Appropriate adjustments to dosage may then be made according to the patient's response.

*Elderly:* Elimination of furosemide is generally slower in the elderly. Dosage should be titrated until the required effect is achieved.

*Paediatric population:* Dosages for children must be determined on the basis of the severity of the renal insufficiency and on the clinical response to initial doses.

Method of administration

Furosemide Injection 20mg/2ml and 50mg/5ml are for intramuscular or for intravenous administration and must always be given slowly. Furosemide Injection 250mg/25ml is for slow intravenous administration.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
Hypersensitivity to amiloride, sulphonamides or sulphonamide derivatives
Hypovolaemia and dehydration (with or without accompanying hypotension) (see section 4.4)
Severe hypokalaemia: severe hyponatraemia (see section 4.4).
Comatose or pre-comatose states associated with hepatic cirrhosis (see section 4.4).
Anuria or renal failure with anuria not responding to furosemide, renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents, renal failure associated with hepatic coma
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).
Digitalis intoxication (see section 4.5).
Porphyria

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.
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.

**Particular caution and/or dose reduction required:**

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.

Elderly people (lower initial dose as particularly susceptible to side-effects - see section 4.2)

difficulty with 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 levels/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. nephritic 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).

**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 people 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 the potassium, 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). A potassium-rich diet is recommended during long-term use.

Frequent checks of the serum potassium are necessary in patients with impaired renal function and creatinine clearance below 60ml/min per 1.73$m^2$ 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
Frequent BUN in first few months of treatment, periodically thereafter. Long-term/high-dose BUN should regularly be measured. Marked diuresis can cause reversible impairment of kidney function in patients with renal dysfunction. 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 triglycerides may rise but usually return to normal within 6 months of starting furosemide.

Concomitant use with risperidone

In risperidone placebo-controlled trials in elderly people 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).

Furosemide 20mg/2ml and 50mg/5ml Solution for Injection contains less than 1mmol sodium (23mg) per 2ml and 5ml ampoules, that is to say essentially 'sodium-free'.

Furosemide 250mg/25ml Solution for Injection contains 91.25mg sodium per 25ml ampoule, equivalent to 4.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

## 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 drugs 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)

**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

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

**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

**Vasodilators** – enhanced hypotensive effect with moxisylyte (thymoxamine) or hydralazine

**Other diuretics** – profound diuresis possible when furosemide given with metolazone.
Increased risk of hypokalaemia with thiazides.

**Renin inhibitors** – aliskiren reduces the 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

**Lithium** - In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with furosemide, resulting 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

**NSAIDs** – increased risk of nephrotoxicity. Indometacin and ketorolac may antagonise the effects of furosemide (avoid if possible see section 4.4). NSAIDs may attenuate the action of furosemide and may cause acute renal failure in cases of pre-existing hypovolaemia or dehydration.

**Salicylates** – effects may be potentiated by furosemide. Salycylic toxicity may be increased by furosemide

**Antibiotics** – increased risk of ototoxicity with aminoglycosides, polymixins or vancomycin - only use concurrently if compelling reasons. Increased risk of nephrotoxicity with aminoglycosides or cefaloridine. 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

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

**Antihistamines** – hypokalaemia with increased risk of cardiac toxicity

**Antifungals** – increased risk of hypokalaemia and nephrotoxicity with amphotericin

**Anxiolytics and hypnotics** – enhanced hypotensive effect. Chloral or triclorfos may displace thyroid hormone from binding site.

**CNS stimulants (drugs used for ADHD)** – hypokalaemia increases the risk of ventricular arrhythmias

**Corticosteroids** – diuretic effect anatgonised (sodium retention) and increased risk of hypokalaemia

**Glychyrrizin** -(contained in liquorice) may and 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 ciclosprin and tacrolimus. Increased risk of gouty arthritis with ciclosporin

**Muscle relaxants** – enhanced hypotensive effect with baclofen or tizanidine. Increased effect of curare-like muscle relaxants

**Oestrogens** – diuretic effect antagonised

**Progestogens (drosperidone)** – increased risk of hyperkalaemia

**Prostaglandins** – enhanced hypotensive effect with alprostadil

**Sympathomimetics** – increased risk of hypokalaemia with high doses of beta$^2$ sympathomimetics

**Theophylline** – enhanced hypotensive effect

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

**Anaesthetic agents** – general anaesthetic agents may enhance the hypotensive effects of furosemide. The effects of curare may be enhanced by furosemide.

**Alcohol** – enhanced hypotensive effect

**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

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. However, furosemide has been given after the first trimester of pregnancy for oedema, hypertension and toxaemia of pregnancy without causing fetal or newborn adverse effects.

Breast-feeding

Furosemide is contraindicated (see section 4.3) as it passes into breast milk and may inhibit lactation.

## 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: Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000, including isolated reports), not known (cannot be estimated from the available data).

The following effects have been reported and are listed below by body system:

| **MedDRA system organ class database** | **Frequency** | **Undesirable effects** |
|---|---|---|

| | | |
|---|---|---|
| Blood and lymphatic system disorders | Uncommon | Thrombocytopenia |
| | Rare | Eosinophilia<br><br>Leukopenia<br><br>Bone marrow depression (necessitates withdrawal of treatment). The haemopoietic status should be therefore be regularly monitored. |
| | Very Rare | Aplastic anaemia or haemolytic anaemia<br>Agranulocytosis |
| Nervous system disorders | Rare | Paraesthesia<br><br>Hyperosmolar coma |
| | Not known | Dizziness, syncope and loss of consciousness (caused by symptomatic hypotension). |
| Eye disorders | Uncommon | Visual disturbance |
| Ear and labyrinth disorders | Uncommon | Deafness (sometimes irreversible) |
| | Rare | Hearing disorders and tinnitus[1] |
| Cardiac disorders | Uncommon: | Cardiac arrhythmias |
| Hepatobiliary disorders | Not known | Cholestasis Intrahepatic (In isolated cases)<br><br>Hepatic encephalopathy in patients with hepatocellular insufficiency may occur (see Section 4.3). |
| Vascular Disorder: | Uncommon | Hypotension[2] |
| | Rare | Vasculitis |
| | Not Known | Thrombosis[8] |
| 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, exfoliative dermatitis, purpura, AGEP (acute generalized exanthematous pustulosis) and DRESS (Drug rash with eosinophilia and systemic symptoms) |
| | Not Known | Bullous Pemphigoid |
| Metabolism and nutrition disorders | Not Known | Symptomatic electrolyte disturbances and Metabolic alkalosis[3]<br><br>Metabolic acidosis[4]<br><br>Hyponatraemia[5]<br><br>Hypokalemia[6]<br><br>Reduction of serum HDL-cholesterol, elevation of serum LDL-cholesterol and elevation of serum triglycerides. During long term therapy they will usually return to normal within six months<br><br>Hypocalcaemia and Hypomagnesemia[7]<br><br>Hypovolaemia and dehydration[8] |
| Psychiatric disorders | Rare | Mental disorder |
| Congenital, familial and genetic disorders | Not Known | Patent ductus arteriosus[9] |
| General disorders and administration site conditions | Uncommon | Fatigue |
| | Rare | Severe anaphylactic or anaphylactoid reactions (e.g. with shock) occurs rarely.<br><br>fever<br><br>Malaise |
| Gastrointestinal disorders | Uncommon | dry mouth, thirst, nausea, bowel motility disturbances, vomiting, diarrhea, constipation[10] |

| | | |
|---|---|---|
| | Rare | Acute Pancreatitis |
| Renal and urinary disorders | Rare | Interstitial nephritis,<br><br>Acute renal failure<br><br>Increased urine production, Urinary incontinence and urinary obstruction[11]<br><br>Acute urine retention[12] |
| | Not known | Nephrocalcinosis/Nephrolithiasis has been reported in premature infants |
| Investigations | Uncommon | Blood creatinine increased and Blood urea increased[13] |
| | Not known | Transaminases increased (In isolated cases)<br><br>Glucose tolerance decreased [14] |

[1]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.

[2] 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.

[3]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 increase excretion of water. In addition, excretion of other electrolytes (in particular potassium, calcium and magnesium) is increased. 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

[4]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.

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

[6]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

[7]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.

[8]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.

[9]If furosemide is administered to premature infants (including those with respiratory distress syndrome) during the first weeks of life, it may increase the risk of persistent patent ductus arteriosus.

[10]Gastro-intestinal disorder such as nausea, malaise or gastric upset (vomiting or diarrhoea) and constipation may occur but not usually severe enough to necessitate withdrawal of treatment.

[11]Increased urine production, urinary incontinence, can be caused or symptoms can be exacerbated in patients with urinary tract obstruction. \

[12]Acute urine retention, possibly accompanied by complications, can occur for example in patients with bladder disorders, prostatic hyperplasia or narrowing of the urethra.

[13]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

[14]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.

*Special population:*

*Patients with hepatic impairment*

Pre-existing metabolic alkalosis (e.g. in decompensated cirrhosis of the liver) may be aggravated by furosemide treatment.

**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 Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

**Symptoms**
Overdose can cause massive diuresis resulting in dehydration, volume depletion and electrolyte disturbances with consequent hypotension and cardiac toxicity. High doses have the potential to cause transient deafness and may precipitate gout (disturbed uric acid secretion).

**Management**
Benefits of gastric decontamination are uncertain. In patients presenting within 1 hour of ingestion, consider activated charcoal (50g for adults: 1g/kg for children)
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. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: High-ceiling diuretic sulfonamides, loop diuretics; ATC code: C03CA01

Mechanism of action:

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.

Pharmacodynamic effects:
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.
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

Absorption:
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 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.

Distribution:
Furosemide is up to 99% bound to plasma proteins.

Biotransformation:
Furosemide is bound to plasma albumin and little biotransformation takes place

Elimination:
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 mainly eliminated via the kidneys (80-90%) 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 the milk.
A small fraction of the dose undergoes biliary elimination and 10-15% of the activity can be recovered from the faeces.

Hepatic impairment
Where liver disease is present, biliary elimination is reduced up to 50%.

Renal impairment
Renal impairment has little effect on the elimination rate of furosemide, but less than 20% residual renal function increases the elimination time.

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

Paediatric population
A sustained diuretic effect is seen in the newborn, possibly due to immature tubular function.

## 5.3 Preclinical safety data

No further information other than that which is contained in other sections of the Summary of Product Characteristics.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Sodium Chloride B.P.
Sodium Hydroxide B.P.
Water for Injections B.P.

### 6.2 Incompatibilities

Furosemide may precipitate solutions of low pH, and therefore dextrose solutions are not suitable infusion fluids for furosemide injection. The injection solution should not be mixed with other drugs in infusion bottles.

### 6.3 Shelf life

3 years.
If only part used, discard the remaining solution.

### 6.4 Special precautions for storage

Keep in outer carton
Do not store above 25°C
Do not refrigerate or freeze.

### 6.5 Nature and contents of container

2ml, 5ml & 25ml One point cut (OPC) amber glass ampoules, glass type 1 Ph.Eur. packed in cardboard cartons to contain 10 x 2ml or 10 x 5ml or 10 x 25ml ampoules.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Limited
Dashwood House,
69 Old Broad Street,
London, EC2M 1QS,
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0576

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24/09/1990
Date of latest renewal:18/06/2003

## 10 DATE OF REVISION OF THE TEXT

26/02/2024