Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Furosemide 250mg in 25ml Solution for Injection/Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of solution contains Furosemide 10mg.
Each 25ml ampoule contains Furosemide 250mg
Excipient with known effect: Each 25ml contains 91 mg (4mmol) sodium

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection/Infusion.
Clear, colourless or almost colourless sterile solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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
Doses of 20 to 50 mg intramuscularly or intravenously may be given initially. If larger doses are required, they should be given increasing by 20 mg increments and not given more often than every two hours. If doses greater than 50 mg are required it is recommended that they be given by slow intravenous infusion. The recommended maximum daily dose of furosemide administration is 1,500 mg.

The recommended initial dose is one 25ml ampoule (250mg) diluted in 225ml Sodium Chloride Injection BP or Ringer's solution for injection, administered over one hour. If urine output is insufficient within the next hour, a dose of two 25ml ampoules (500mg) in an appropriate infusion fluid may be given over two hours. The total volume of the infusion should be governed by the patient's state of hydration. If a satisfactory urine output has still not been achieved within one hour of the end of the second infusion, a third infusion containing four 25ml ampoules (1,000mg) may be given. The rate of infusion should not exceed 4mg/minute.

In oliguric or anuric patients with significant fluid overload, the injection may be given without dilution directly into the vein, using a constant-rate infusion pump with a micrometer screw-gauge adjustment; the rate of administration should still not exceed 4mg/minute. If the response to either method of administration is satisfactory, then the effective dose (of up to 1g) may be repeated every 24 hours. Dosage adjustments should subsequently be made according to the patient's response. Alternatively, the oral route may be used for maintenance therapy and 500mg may be given by mouth for each 250mg required by injection. Patients who do not respond to a third infusion, using the maximum intravenous dose of 1g over four hours, probably require dialysis.

Elderly: The dosage recommendations for adults apply, but in the elderly furosemide is generally eliminated more slowly. Dosage should be titrated until the required response is achieved.

Paediatric population: Parenteral doses for children range from 0.5 to 1.5 mg/kg body weight daily up to a maximum total daily dose of 20 mg. Doses for children can only be determined on the basis of the severity of the renal insufficiency and the clinical response to initial doses.

Method of administration
Route of administration: intramuscular or intravenous

Intravenous furosemide must be injected or infused slowly; a rate of 4 mg per minute must not be exceeded. In patients with severe impairment of renal function (serum creatinine>5 mg/dl), it is recommended that an infusion rate of 2.5 mg per minute is not exceeded.

Intramuscular administration must be restricted to exceptional cases where neither oral nor intravenous administration are feasible. It must be noted that intramuscular injection is not suitable for the treatment of acute conditions such as pulmonary oedema.

To achieve optimum efficacy and suppress counter-regulation, a continuous furosemide infusion is generally to be preferred to repeated bolus injections. Where continuous furosemide infusion is not feasible for follow-up treatment after one or several acute bolus doses, a follow-up regimen with low doses given at short intervals (approx. 4 hours) is to be preferred to a regimen with higher bolus doses at longer intervals.

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 patients (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 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 1.73m^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 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).

This medicinal product contains 91 mg 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 new born adverse effects.

Breast-feeding
Furosemide is contraindicated (see section 4.3) as it passes into breast milk and may 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: Uncommon (≥ 1/1,000, < 1/100), rare (≥ 1/10,000, < 1,000) and 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 Leukopenia Bone marrow depression (necessitates withdrawal of treatment). The haemopoietic status should be therefore be regularly monitored.
	Very Rare	Aplastic anaemia or haemolytic anaemia Agranulocytosis

Metabolism and nutrition disorders	Very Rare	Hypocalcaemia and Hypomagnesemia[1]
	Not Known	Symptomatic electrolyte disturbances and Metabolic alkalosis[2] Metabolic acidosis[3] Hyponatraemia[4] Hypokalemia[5] 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 Hypovolaemia and dehydration[6]
Psychiatric disorders	Rare	Mental disorder
Nervous system disorders	Rare	Paraesthesia 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[7]
Cardiac disorders	Uncommon	Cardiac arrhythmias
Vascular disorders	Uncommon	Hypotension[8]
	Rare	Vasculitis
	Not known	Thrombosis[6]
Gastrointestinal disorders	Uncommon	Dry mouth, thirst, nausea, Gastrointestinal motility disorder, vomiting, diarrhoea, constipation[9]
	Rare	Acute Pancreatitis
Hepatobiliary disorders	Not known	Cholestasis intrahepatic (In isolated cases) Hepatic encephalopathy in patients with hepatocellular insufficiency may occur (see Section 4.3)
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
Renal and urinary disorders	Rare	Tubulointerstitial nephritis, Acute renal failure Increased urine production, Urinary incontinence[10] Acute urine retention[11]
	Not known	Nephrocalcinosis/Nephrolithiasis has been reported in premature infants
Congenital, familial and genetic disorders	Not Known	Patent ductus arteriosus[12]
General disorders and administration site conditions	Uncommon	Fatigue
	Rare	Severe anaphylactic or anaphylactoid reactions (e.g. with shock) fever Malaise
Investigations	Uncommon	Blood creatinine increased and Blood urea increased[13]
	Not known	Transaminases increased (In isolated cases) Glucose tolerance decreased [14]

[1] 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.

[2] 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

[3] 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.

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

[5] 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

[6] 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.

[7] 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.

[8] 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.

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

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

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

[12] If furosemide is administered to premature infants or in premature infants with respiratory distress syndrome during the initial weeks after birth entails an increased risk of a persistent patent ductus arteriosus.

[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.

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 HPRA Pharmacovigilance, Website: www.hpra.ie.

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: C03C A01

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
Sodium Hydroxide (for pH adjustment)
Water for Injection

6.2 Incompatibilities

Furosemide may precipitate in solutions of low pH and therefore, Dextrose solutions are not suitable infusion fluids for Furosemide Injection. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

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

6.4 Special precautions for storage

Do not store above 25°C
Keep ampoules in the outer carton in order to protect from light.
Do not refrigerate or freeze.

6.5 Nature and contents of container

25 ml, amber glass ampoules, glass type 1 Ph. Eur. borosilicate glass, packed in cardboard cartons to contain 10 x 25ml ampoules.

6.6 Special precautions for disposal and other handling

For single use only. If only part used, discard the remaining solution.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals (Ireland) Ltd
4045 Kingswood Road
Citywest Business Park
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Ireland

8 MARKETING AUTHORISATION NUMBER

PA0073/059/006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 May 1990

Date of last renewal: 28 May 2010

10 DATE OF REVISION OF THE TEXT

April 2024