Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Furosemide Injection BP Minijet 10mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 10 mg of the active substance Furosemide.

Excipient(s) with known effect:

Each ml of solution contains 7.5 mg of sodium chloride (corresponding to 2.95 mg/ml of sodium).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
A clear, colourless, sterile aqueous solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Conditions requiring prompt diuresis, where oral therapy is precluded.

Indications include oedema of cardiac, pulmonary, hepatic or renal origin, forced diuresis and severe hypercalcaemia.

4.2 Posology and method of administration

Parenteral administration should be replaced with oral therapy as soon as possible.

The intravenous injection should be given slowly (maximum 4mg/minute). Usually a prompt diuresis ensues.

Adults:

Acute pulmonary oedema: 40mg should be given immediately by slow intravenous injection, followed by further doses depending upon the patient's response. If there is no satisfactory response within 1 hour, 80mg may be given slowly intravenously.

Oedema: The usual initial dose of furosemide is 20 to 40mg given as a single dose, injected intravenously or intramuscularly.

If the diuretic response with a single dose of 20 to 40mg is not satisfactory, the dose may be increased in 20mg increments at 2 hourly intervals until the desired diuretic effect is obtained.
Very high doses may be required in patients with renal failure (see below).

Hypercalcaemia: Doses ranging from 20-240mg daily have been used. The aim is to increase diuresis to about 6 litres daily.

Forced diuresis: intravenous isotonic fluid at the rate of 500ml/hour is administered together with repeated doses of 20-80mg furosemide to produce a diuresis of 11-12 litres daily.

Acute or chronic renal failure: To avoid ototoxicity furosemide should be administered by intravenous infusion at a rate not exceeding 4mg/minute. The recommended initial dose in patients with acute or chronic renal failure is 25ml (250mg), diluted in approximately 225ml Sodium Chloride Injection BP or Ringer's Solution for Injection, administered over one hour. This gives an approximate drip rate of 80 drops/minute ensuring that the infusion is at the rate of 4mg/minute.

If a satisfactory increase in urine output, such as 40-50ml/hour, is not attained within the next hour, a second infusion of 50ml (500mg) in an appropriate infusion fluid should be given over 2 hours, the total volume of the infusion being governed by the patient's state of hydration. If a satisfactory output is still not achieved within one hour of the end of the second infusion, a third infusion of 100ml (1000mg) can be given over 4 hours. If the third infusion is not effective, then dialysis will probably be required.

In oliguric or anuric patients with significant fluid overload it may not be practicable to administer high dose furosemide by the above method. Under these circumstances the use of a constant rate infusion pump with micrometer screw-gauge adjustment may be considered for direct administration of the injection into the vein.

If the furosemide infusion produces a satisfactory response of 40-50ml/hour, the effective dose (up to 1000mg) can be repeated every 24 hours. Alternatively maintenance therapy can be continued with oral furosemide. Approximate dosage adjustments may then be made according to the observed clinical response.

Elderly: As for adults; the dose should be kept as low as possible.

Children: The usual initial dose is 0.5-1.5mg/kg up to 20mg/day. If the diuretic response after the initial dose is not satisfactory, the dose may be increased by 1mg/kg at 2 hourly intervals until the desired effect has been obtained. Doses greater than 6mg/kg are not recommended. For maintenance therapy, the dosage should be adjusted to the minimum effective level.

4.3 Contraindications

Furosemide is contra-indicated in women of child-bearing potential because animal reproductive studies have shown that it may cause foetal abnormalities. Exceptions to the above are life-threatening situations where the use of a diuretic such as furosemide is especially indicated as opposed to the use of alternative drugs. The physician of course should balance this efficacy potential against teratogenic and embryotoxic potential demonstrated to occur in animal studies.

Furosemide is contraindicated in patients with known hypersensitivity to the drug or to sulfonamides, renal failure associated with anuria or hepatic coma and in the presence of severe sodium and fluid depletion.

4.4 Special warnings and precautions for use

Fluid balance should be carefully monitored. Furosemide may cause profound diuresis, resulting in fluid and electrolytedepletion. Serum electrolytes (especially sodium, potassium, chloride and bicarbonate) should be determined, andabnormalities corrected or the drug withdrawn. If increasing azotemia and oliguria occur during the treatment ofprogressive renal disease, the drug should be discontinued.

Initiation of furosemide therapy in patients with hepatic cirrhosis and ascites is best carried out in hospital. Suddenalteration of fluid and electrolyte balance in patients with cirrhosis may precipitate hepatic coma, therefore strictobservation is necessary during the period of diuresis.

Patients should be regularly observed for the possible occurrence of blood dyscrasias, liver damage or otheridiosyncratic reactions.

Periodic checks on urine and blood glucose should be made in diabetics and those suspected of latent diabetes whenreceiving furosemide. Increases in blood glucose and alterations in glucose tolerance test, with abnormalities of thefasting and 2-hour post-prandial sugar have been observed and rare cases of precipitation of diabetes mellitus have beenreported.

Furosemide may lower serum calcium levels and rare cases of tetany have been reported. Accordingly, calcium shouldbe determined periodically.

Patients with prostatic hypertrophy or impaired micturition have an increased risk of developing acute retention.

Care is advised when prescribing Furosemide to patients with either gout or porphyria.

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.

4.5 Interaction with other medicinal products and other forms of interactions

Furosemide-induced hypokalemia may induce potentially fatal cardiac arrhythmias during treatment with cardiac glycosides or drugs that prolong the Q.T. interval (e.g. amiodarone or fluconazole).

Furosemide may increase the toxicity of aminoglycoside antibiotics. Furosemide may enhance the nephrotoxicity of cephalosporins.

Due to diuretic-induced sodium depletion, renal clearance of lithium is reduced, which may result in increased lithium concentrations leading to lithium toxicity.

Fluid retention caused by steroids may potentially antagonize the diuretic effect but potentiate the potassium loss.

In oedematous hypertensive patients being treated with antihypertensive agents, care should be taken to reduce the dose of these drugs since furosemide potentiates the hypotensive effect. Severe hypotension and/or renal failure may occur if treatment with angiotensin- converting enzyme inhibitors is initiated while patients are receiving high doses of loop diuretics. The dose of furosemide should be reduced and severe salt and water depletion corrected before starting the ACE-inhibitor.

Sulfonamide diuretics have been reported to decrease arterial responsiveness to pressor amines and to enhance the effect of tubocurarine. Great caution should be exercised in administering curare or its derivatives to patients undergoing therapy with furosemide and it is advisable to discontinue furosemide two days before elective surgery.

Non-steroidal anti-inflammatory drugs may partially antagonise the action of furosemide. Because of competition for renal excretion, patients receiving high doses of salicylates together with furosemide may experience salicylate toxicity.

The following drugs have been reported to result in a disturbance in the electrolyte balance if given concurrently with furosemide: hormone antagonists, sympathetomimetics, carbamazepine, metalozone; and ulcer healing drugs (e.g. carbenoxolone).

Estrogens, probenicid and lipid lowering resins may result in reduction in the diuretic effects of furosemide if administered concurrently. Attenuation of the effect of furosemide may occur following concurrent administration of phenytoin and other antiepileptics.

Flushing, tachycardia, elevated blood pressure and severe diaphoresis have been seen in patients receiving intravenous furosemide having taken oral chloral hydrate in the preceding 24 hours.

Concurrent administration of furosemide and clofibrate may result in marked diuresis and muscle symptoms in patients with marked nephrotic syndrome.

The muscle relaxants baclofen and izanidine may increase the hypotensive effect of furosemide.

Furosemide may enhance the hyperglycaemic action of diazoxide.

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

Liquorice, prolonged use of laxatives, reboxetine, amphotericin and use of thiazide diuretics may increase the risk of developing hypokalemia.

4.6 Fertility, pregnancy and lactation

Animal teratology studies indicate that furosemide may cause foetal abnormalities. Therefore, furosemide should only be used in women of child-bearing age when appropriate contraceptive measures are taken or if the potential benefits justify the potential risks to the foetus.

Furosemide is excreted in breast milk and breast-feeding should be discontinued if treatment is essential.

4.7 Effects on ability to drive and use machines

Furosemide may reduce mental alertness. Patients should be warned not to drive or operate machinery if affected.

4.8 Undesirable effects

Excessive diuresis may result in dehydration and reduction in blood volume, with circulatory collapse and with thepossibility of vascular thrombosis and embolism, particularly in elderly patients. Serious depletion of potassium andmagnesium may lead to cardiac arrhythmias.

Electrolyte depletion may manifest itself by weakness, fatigue, light-headedness or dizziness, muscle cramps, thirst,increased perspiration, fever, urinary bladder spasm and symptoms of urinary frequency.

Transient pain after intramuscular injection has been reported at the injection site. Thrombophlebitis has occurred withintravenous IV administration.

Various forms of dermatitis, including urticaria and rare cases of exfoliative dermatitis, erythema multiforme, pruritus,paraesthesia, blurring of vision, postural hypotension, nausea, vomiting or diarrhoea, photosensitivity, or hypersensitivityreactions, including vasculitis/arteritis, bullous pemphigoid or vesiculobullous eruptions may occur. Anaemia, leucopenia,aplastic anaemia and thrombocytopenia (with purpura) may occur. Very rarely, agranulocytosis has occurred which hasresponded to treatment. If a rash or thrombocytopenia occur, furosemide should be stopped immediately.

Cases of tinnitus and reversible hearing impairment have been reported. There have also been some reports of cases inwhich hearing impairment was irreversible. Usually ototoxicity is associated with rapid injection in patients with severerenal impairment at doses several times more than the usual recommended dose and in whom other drugs of knownototoxicity were given.

Acute diuresis in male patients with prostatic obstruction may cause acute retention of urine.

In addition, the following rare adverse events have been reported although the relationship to the drug has not beenconfirmed: sweet taste, oral and gastric burning, paradoxical swelling, headache, jaundice, and acute pancreatitis.

In children, complaints of mild to moderate abdominal pain and cramping have been reported after intravenous furosemide.Nephrocalcaemia has been reported in premature infants.

Asymptomatic hyperuricaemia can occur and rarely gout may be precipitated. These are associated with dehydration whichshould be avoided particularly in patients with renal insufficiency.

Nervous system disorders (frequency not known): dizziness, fainting and loss of consciousness (caused by symptomatic hypotension).

Skin and subcutaneous tissue disorders (frequency not known): acute generalised exanthematouspustulosis (AGEP)

Ear and labyrinth Disorders (frequency uncommon): deafness (sometimes irreversible)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continuedmonitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report anysuspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax:+353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms: Overdose with furosemide may lead to excessive loss of water and electrolytes. Severe potassium loss may cause serious cardiac arrhythmias.

Treatment: Restoration of fluid and electrolytes balance by administration of sodium chloride and water, intravenously if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Furosemide is a short-acting sulfonamide diuretic, chemically similar to the thiazides. With parenteral administration, the diuretic effect is immediate and lasts approximately two hours. Furosemide primarily inhibits the reabsorption of sodium in the proximal and distal tubules as well as in the Loop of Henle, thus increasing the urinary excretion of sodium, chloride and water. Urinary excretion of potassium, calcium and magnesium are also increased, together with bicarbonate; urinary pH rises.

5.2 Pharmacokinetic properties

Furosemide is 91% to 99% bound to serum albumin but protein binding is reduced in patients with uraemia and nephrosis. The plasma half life ranges from 45 to 60 minutes. Furosemide crosses the placenta and enters breast milk. It is eliminated by renal excretion of unchanged drug, metabolism to a glucuronide conjugate and faecal excretion.

5.3 Preclinical safety data

Toxicity studies in animals have not demonstrated toxic effects relevant to clinical use. There is no evidence of mutagenic or carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide (for pH adjustment)
Sodium chloride
Water for injections

6.2 Incompatibilities

Furosemide is soluble in alkaline solutions. The injection is a mildly buffered alkaline solution which should not be mixed with highly acidic solutions.

6.3 Shelf life

Unopened: 3 years.
For single use only.
Discard any remaining contents after first use.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the vial in the outer carton.

6.5 Nature and contents of container

A Type I glass vial with an elastomeric closure, packed together with a sterile disposable syringe (Min-I-Jet system) in a sealed unit carton. Each vial contains 8 ml of solution.

6.6 Special precautions for disposal

The container is specially designed for use with the IMS Min-I-Jet injector.

7 MARKETING AUTHORISATION HOLDER

DLRC Pharma Services Limited
Chesterfield House
Clonmannon

Ashford
Wicklow
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22684/006/001

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Date of first authorisation: 11 January 1990

Date of last renewal: 11 January 2010

10 DATE OF REVISION OF THE TEXT

May 2019