PROFESSIONAL INFORMATION

SCHEDULING STATUS S3

1 NAME OF THE MEDICINE

PHARMA-Q FUROSEMIDE INJECTION 20 mg/2 ml solution for injection.

PHARMA-Q FUROSEMIDE INJECTION 50 mg/5 ml solution for injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

PHARMA-Q FUROSEMIDE INJECTION 20 mg/2 ml:

Each 1 ml solution or injection contains 10 mg furosemide.

Each 2 ml ampoule contains 20 mg furosemide.

PHARMA-Q FUROSEMIDE INJECTION 50 mg/5 ml:

Each 1 ml solution for injection contains 10 mg furosemide.

Each 5 ml ampoule contains 50 mg furosemide.

Sugar free

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection

A clear, colourless to almost colourless solution, in 2 ml or 5 ml amber ampoules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

PHARMA-Q FUROSEMIDE INJECTION is indicated for the treatment of:

- Cardiac oedema.
- Acute Pulmonary oedema.
- Renal or hepatic oedema.
- Cerebral oedema.
- Conditions of fluid overloaded when IV therapy is indicated.

4.2 Posology and method of administration

Posology

Intravenous or intramuscular administration of PHARMA-Q FUROSEMIDE INJECTION is indicated where intestinal absorption is impaired or prompt diuresis is required.

The recommended dose for adults is:

- Intramuscular or intravenous dose of 20 mg to 50 mg, repeated if necessary after not less than 2 hours.
- Intravenous injection should be given slowly.
- The rate must not exceed 4 mg per minute.

The usual paediatric dose for infants and children under 15 years) is:

- Intravenous dose of 0,5 to 1,5 mg/kg body mass per day up to a maximum of 20 mg per day.

- Intravenous injection should be given slowly.
- The rate must not exceed 4 mg per minute.
- Should be used parenterally (if necessary, continuous drip infusion) only in life-threatening situations.

Other doses:

- **Pulmonary oedema**: Initial dose is 40 mg intravenously given slowly.
- If necessary, the injection may be repeated after approximately 60 minutes.
- The dose may be increased to 80 mg, given slowly intravenously.

Method of Administration:

PHARMA-Q FUROSEMIDE INJECTION**:**

- Should be injected slowly when administered intravenously.
- The rate of injection of 4 mg per minute should not be exceeded.
- During long-term treatment, serum creatinine, urea, electrolytes, in particular potassium, calcium, chloride and bicarbonate, should be regularly checked.
- Furosemide is an anthranilic acid derivative and dissolves in alkaline media with salt formation.
- The solution for parenteral application contains the sodium salt of the carboxylic acid without a solubiliser.
- The solution has a pH of about 9 but no buffer capacity, which means that the medicine may precipitate at pH values below 7.
- If the ready-to-use solution has a pH ranging from weakly alkaline to neutral, the mixture

may be used for up to 24 hours.

- PHARMA-Q FUROSEMIDE INJECTION must not be mixed with other medicines in the same injection syringe.
- The duration of treatment is at the doctor's discretion.

4.3 Contraindications

- Hypersensitivity to furosemide, amiloride, sulphonamides, sulphonamide derivatives (cross-sensitivity exists between sulphonamides and furosemide) or to any of the excipients listed in section 6.1.
- 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).
- Pregnancy and lactation (see section 4.6).
- PHARMA-Q FUROSEMIDE INJECTION should not be given in anuria or in renal failure due to nephrotoxic or hepatotoxic medicines nor in renal failure associated with hepatic coma.
- Impaired renal function with a creatinine clearance below 30 ml/min per 1,73 m^2 body surface area.
- PHARMA-Q FUROSEMIDE INJECTION should not be given to patients with Addison's disease or pre-existing hypercalcaemia.
- Digoxin intoxication (see section 4.5).
- Porphyria.

4.4 Special warnings and precautions for use

Conditions requiring correction before treatment with PHARMA-Q FUROSEMIDE INJECTION is started (also see section 4.3):

- Hypotension.
- Hypovolaemia.
- Severe electrolyte disturbances – particularly hypokalaemia, hyponatraemia and acid-base disturbances. Fluid and electrolyte imbalance should be monitored during therapy.

PHARMA-Q FUROSEMIDE INJECTION 20 mg/2 ml and PHARMA-Q FUROSEMIDE INJECTION 50 mg/5 ml solution for injection contain less than 1 mmol sodium (23 mg) per 2 ml and per 5 ml ampoules, that is to say essentially 'sodium-free'.

PHARMA-Q FUROSEMIDE INJECTION is not recommended:

- In patients at high risk for radiocontrast nephropathy – PHARMA-Q FUROSEMIDE INJECTION should not be used for diuresis as part of the preventative measures against radiocontrast-induced nephropathy. Except as a single trial dose in acute anuria in the absence of obstruction, PHARMA-Q FUROSEMIDE INJECTION should be avoided in anuric patients.

Particular caution and/or dose reduction required:

- Symptomatic hypotension leading to dizziness, fainting or loss of consciousness can occur in patients treated with PHARMA-Q FUROSEMIDE INJECTION, particularly in the elderly, patients using other medicines which can cause hypotension, and patients with other medical

conditions that are risks for hypotension.

- Elderly people (lower initial dose as they may be 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 PHARMA-Q FUROSEMIDE INJECTION before a glucose tolerance test).
- Pregnancy (see sections 4.3 and 4.6).
- Patients with hepatorenal syndrome.
- Caution should be exercised in patients with impaired hepatic function or renal impairment (see section 4.3 and below – monitoring required).
- PHARMA-Q FUROSEMIDE INJECTION may enhance the nephrotoxicity of cephalosporin and aminoglycoside antibiotics (see section 4.5).
- Hypoproteinaemia e.g. nephritic syndrome (effect of PHARMA-Q FUROSEMIDE INJECTION, may be impaired and its ototoxicity potentiated – cautious dose titration is required).
- Acute hypercalcaemia (dehydration results from vomiting and diuresis – should be corrected before giving PHARMA-Q FUROSEMIDE INJECTION). Treatment of hypercalcaemia with a high dose of furosemide results in fluid and electrolyte depletion – meticulous fluid replacement and correction of electrolytes are required.
- Patients who are at risk from a pronounced fall in blood pressure.
- PHARMA-Q FUROSEMIDE INJECTION has been associated with acute attacks of porphyria and is considered unsafe in porphyria patients (see section 4.3).

- Caution should be exercised in patients with gout (furosemide, as in PHARMA-Q FUROSEMIDE INJECTION, may raise uric acid levels/precipitate gout).
- Patients on restricted sodium intake are particularly susceptible to excessive dehydration and hypotension.
- Patients sensitive to sulphonamides may develop allergic dermatological and vasculitic reactions to PHARMA-Q FUROSEMIDE INJECTION (see section 4.3).
- Caution must be exercised in administering PHARMA-Q FUROSEMIDE INJECTION to infants, particularly for extended periods. In premature infants there is a possibility of developing nephrocalcinosis or nephrolithiasis (renal function must be monitored, and renal ultrasonography performed).

Laboratory monitoring requirements:

Serum sodium

Particularly in 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 digoxin 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 60 ml/min per 1,73 m^2 body surface area, as well as in cases where furosemide is taken in combination with certain other medicines which may lead to an increase in potassium levels (see section 4.5 and refer to section 4.8 for details of electrolyte and metabolic abnormalities).

Renal function

Frequent blood urea nitrogen (BUN) in the 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 hypomagnesaemia (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 (also see section 4.8):

Regular monitoring for blood dyscrasias. If these occur, stop PHARMA-Q FUROSEMIDE INJECTION immediately:

- liver damage
- idiosyncratic reactions.

Other alterations in laboratory values

- Serum cholesterol and triglycerides may rise but usually return to normal within 6 months of starting PHARMA-Q FUROSEMIDE INJECTION.
- Concomitant use with risperidone (see section 4.5).

  In risperidone placebo-controlled trials in elderly people with dementia, a higher incidence of mortality was observed in patients treated with furosemide plus risperidone, when compared to patients treated with risperidone alone or furosemide alone. 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).

4.5 Interaction with other medicines and other forms of interaction

General: The dosage of concurrently administered digoxin, diuretics, antihypertensives or other medicines with blood pressure-lowering potential may require adjustment, as a more pronounced fall in blood pressure must be anticipated if given concomitantly with PHARMA-Q FUROSEMIDE INJECTION**.**

PHARMA-Q FUROSEMIDE INJECTION may enhance the nephrotoxicity of cephalosporin antibiotics and can enhance the ototoxicity of aminoglycoside antibiotics and other ototoxic medicines.

Neuromuscular blockers – the neuromuscular blocking action of competitive neuromuscular blockers, such as atracurium, may be enhanced.

Antihypertensives – enhanced hypotensive effect possible with all types. Concurrent use with angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists can result in marked falls in blood pressure, PHARMA-Q FUROSEMIDE INJECTION 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 dysrhythmias 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 regarding increased mortality in elderly patients with dementia concomitantly receiving risperidone.

Antidysrhythmics (including amiodarone, disopyramide, flecainide and sotalol) – risk of cardiac toxicity (because of furosemide-induced hypokalaemia).

Lidocaine (lignocaine), tocainide or mexiletine – the effects of lidocaine (lignocaine), tocainide or mexiletine may be antagonised by furosemide, as in PHARMA-Q FUROSEMIDE INJECTION.

Digoxin – hypokalaemia and electrolyte disturbances (including hypomagnesaemia) increase the risk of cardiac toxicity.

Medicines that prolong QT interval – increased risk of toxicity with furosemide- induced electrolyte disturbances.

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

Other diuretics – profound diuresis is possible when furosemide, as in PHARMA-Q FUROSEMIDE INJECTION, is given with metolazone. Increased risk of hypokalaemia with thiazides.

Renin inhibitors – aliskiren reduces plasma concentrations of furosemide, as in PHARMA-Q

FUROSEMIDE INJECTION.

Nitrates – enhanced the hypotensive effect of PHARMA-Q FUROSEMIDE INJECTION.

Alcohol, barbiturates or opioids – orthostatic hypotension associated with PHARMA-Q FUROSEMIDE INJECTION may be enhanced by alcohol, barbiturates or opioids.

Nonsteroidal anti-inflammatory drugs (NSAIDs) – the antihypertensive effect may be antagonised by medicines that cause fluid retention, such as nonsteroidal anti-inflammatory drugs (NSAIDs). The nephrotoxicity of NSAIDs may be enhanced. Indomethacin and ketorolac may antagonise the effects of furosemide (avoid, if possible, see section 4.4). NSAIDs may attenuate the action of furosemide, as in PHARMA-Q FUROSEMIDE INJECTION, and may cause acute renal failure in cases of pre-existing hypovolaemia or dehydration.

Lithium – PHARMA-Q FUROSEMIDE INJECTION should not be used with lithium.

Allopurinol – the toxicity of allopurinol may be increased.

Tetracycline antibiotics – the toxicity of tetracyclines may be increased.

Chelating medicines – sucralfate may decrease the gastrointestinal absorption of furosemide, as in PHARMA-Q FUROSEMIDE INJECTION. Sucralfate and PHARMA-Q FUROSEMIDE INJECTION should be used at least 2 hours apart.

Salicylates – the effects of salicylates may be potentiated by furosemide, as in PHARMA-Q FUROSEMIDE INJECTION. Salicylic toxicity may be increased by PHARMA-Q FUROSEMIDE INJECTION.

Antibiotics – increased risk of ototoxicity with aminoglycosides, polymyxins or vancomycin; only use concurrently if there are compelling reasons. Increased risk of nephrotoxicity with aminoglycosides or cefaloridine. Furosemide, as in PHARMA-Q FUROSEMIDE INJECTION, 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 monoamine oxidase inhibitors (MAOIs). Increased risk of postural hypotension with tricyclic antidepressants (TCAs). Increased risk of hypokalaemia with reboxetine.

Antidiabetics – PHARMA-Q FUROSEMIDE INJECTION may alter the requirements for hypoglycaemics in diabetic patients.

Antiepileptics – increased risk of hyponatraemia with carbamazepine. Concurrent administration of phenytoin may reduce the clinical effects of PHARMA-Q FUROSEMIDE INJECTION.

Antihistamines – hypokalaemia with increased risk of cardiac toxicity.

Antifungals – increased risk of hypokalaemia and nephrotoxicity with amphotericin.

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

Central nervous system (CNS) stimulants (medicines used for attention deficit hyperactivity disorder (ADHD)) – hypokalaemia increases the risk of ventricular dysrhythmias.

Corticosteroids and corticotrophin – diuretic effect antagonised (sodium retention) and increased risk of hypokalaemia.

Glycyrrhizin – (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 PHARMA-Q FUROSEMIDE INJECTION 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.

Antimetabolites – effects of PHARMA-Q FUROSEMIDE INJECTION may be reduced by methotrexate and PHARMA-Q FUROSEMIDE INJECTION 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.

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 beta2 sympathomimetics, such as salbutamol.

Theophylline – enhanced hypotensive effect.

Probenecid – effects of PHARMA-Q FUROSEMIDE INJECTION may be reduced by probenecid, and furosemide, as in PHARMA-Q FUROSEMIDE INJECTION**,** may reduce renal clearance of probenecid.

Anaesthetic medicines – general anaesthetic medicines may enhance the hypotensive effects of furosemide. The effects of curare may be enhanced by PHARMA-Q FUROSEMIDE INJECTION.

Laxative abuse – increases the risk of potassium loss.

Others – concomitant administration of aminoglutethimide may increase the risk of hyponatraemia.

The response of pressor amines e.g. noradrenaline (norepinephrine), has been reported to be diminished.

4.6 Fertility, pregnancy and lactation

The safety of PHARMA-Q FUROSEMIDE INJECTION in pregnancy and lactation has not been established (see section 4.3).

PHARMA-Q FUROSEMIDE INJECTION should not be used during pregnancy and lactation since it crosses the placenta and also appears in breast milk. PHARMA-Q FUROSEMIDE INJECTION may compromise placental perfusion by reducing maternal blood volume; it may also inhibit lactation.

4.7 Effects on ability to drive and use machine

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 a vehicle, operate machinery or take part in activities where

these effects could put themselves or others at risk.

4.8 Undesirable effects

System Organ Class	Frequency	Undesirable effects
Blood and the lymphatic system disorders	Less Frequent	Bone marrow depression (necessitates withdrawal of treatment, the haemopoietic status should therefore be regularly monitored), aplastic anaemia or haemolytic anaemia, agranulocytosis, thrombocytopenia, leukopenia, and eosinophilia Electrolyte imbalance: hyponatraemia, hypokalaemia[2] and hypochloraemic alkalosis particularly after large doses or prolonged administration
Immune system disorders	Less Frequent	Allergy Hypersensitivity reactions including interstitial nephritis and fever
Endocrine disorders	Frequency unknown	Hyperglycaemia and glycosuria. Hyperuricaemia (with precipitated attacks of gout) Increased excretion of calcium

		Glucose tolerance decreased[1]
Metabolism and nutrition disorders	Frequency unknown	Electrolyte imbalance: hypovolaemic shock
Nervous system disorders	Less Frequent	Paraesthesia Hyperosmolar coma
	Frequency unknown	Dizziness, headache, fainting and loss of consciousness (caused by symptomatic hypotension) Electrolyte imbalance: headache, lethargy and restlessness
Eye disorders	Less Frequent	Visual disturbance
	Frequency unknown	Blurred vision, yellow vision
Ear and labyrinth disorders	Less frequent	Tinnitus and deafness[2]
Cardiac disorders	Less frequent	Cardiac dysrhythmias Hypotension[3] Hypovolaemia and dehydration[4]
Vascular disorders	Less frequent	Vasculitis
Gastrointestinal disorders	Less frequent	Nausea, vomiting, diarrhoea, constipation, acute pancreatitis Electrolyte imbalance: dry mouth, thirst and gastrointestinal

		disturbances
Hepato-biliary disorders	Frequency unknown	Jaundice, hepatic dysfunction and cholestatic jaundice Intrahepatic cholestasis (isolated cases) Increase in liver transaminases or acute pancreatitis may develop Hepatic encephalopathy in patients with hepatocellular insufficiency may occur (see section 4.3)
Skin and subcutaneous tissue disorders	Less frequent	Photosensitivity and skin rashes 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 generalised exanthematous pustulosis) and DRESS (drug rash with eosinophilia and systemic symptoms)
	Frequency unknown	Bullous pemphigoid

Musculoskeletal and connective tissue disorders	Frequency unknown	Electrolyte imbalance: muscle cramps and weakness
Renal and urinary disorders	Less frequent	Serum creatinine and urea levels can be temporarily elevated Interstitial nephritis Acute renal failure Increased urine production and urinary incontinence and urinary tract obstruction[5] Acute urine retention[6]
	Frequency unknown	Renal stone formation when used to treat preterm infants Electrolyte imbalance: dehydration and oliguria
Pregnancy, puerperium and perinatal conditions	Frequency unknown	Patent ductus arteriosus[7] Nephrocalcinosis (renal stone formation when used to treat preterm infants) Rare complications may include minor psychiatric disturbances

[1]Glucose tolerance may decreased with PHARMA-Q FUROSEMIDE INJECTION. 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.

[2]Tinnitus and deafness may occur during rapid, high-dose therapy (faster than 4 mg/minute), although usually transitory, it may occur in rare cases, particularly in patients with renal failure or hypoproteinaemia (e.g. in nephritic syndrome). Deafness may be permanent, particularly in patients with impaired renal function or when administered concomitantly with ototoxic medicine.

[3]PHARMA-Q FUROSEMIDE INJECTION 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 and orthostatic intolerance.

[4]The diuretic effect of PHARMA-Q FUROSEMIDE INJECTION can result in hypovolaemia and dehydration, especially in the elderly. There is an increased risk of thromboses.

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

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

[7]If PHARMA-Q FUROSEMIDE INJECTION is administered to premature infants (including those with respiratory distress syndrome) in the first initial weeks after birth, it may increase the risk of persistent patent ductus arteriosus.

Special population:

Patients with hepatic impairment

Pre-existing metabolic alkalosis: Patients with underlying disorders (e.g. in decompensated cirrhosis of the liver or heart failure) may be at higher risk for this side effect.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of PHARMA-Q FUROSEMIDE INJECTION is important. It allows continued monitoring of the benefit/risk balance of PHARMA-Q FUROSEMIDE INJECTION. Health care providers are requested to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

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).

Treatment

Benefits of gastric decontamination are uncertain. In patients presenting within 1 hour of ingestion, consider activated charcoal (50 g for adults and 1 g/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 electrocardiogram (ECG) in patients with significant electrolyte disturbances.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 18.1 Diuretics.

Pharmacotherapeutic group: High-ceiling diuretic sulphonamides, loop diuretics

ATC code: C03CA01.

Mechanism of action:

The principal renal action of furosemide is to inhibit active chloride transport in the thick ascending limb.

Re-absorption of sodium and chloride from the nephron is reduced, and a hypotonic or isotonic urine produced.

Furosemide is a high-ceiling diuretic acting primarily by inhibiting electrolyte reabsorption in the thick ascending limb of the loop of Henle, as well as in the proximal tubule. 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:

It has a rapid onset of action when administered parenterally. Approximately 65 % of the dose is absorbed after oral administration. It has a biphasic half-life with a terminal elimination phase of about 1,5 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 albumin.

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 furosemide 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. A small fraction of the dose undergoes biliary elimination and 10 – 15 % of the activity can be recovered from the faeces.

Furosemide crosses the placental barrier and is excreted in the milk.

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.

Elderly patients:

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

Newborn patients:

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (37 % solution) (pH adjuster)
Sodium chloride
Sodium hydroxide
Water for injection.

6.2 Incompatibilities

The solution has a pH of about 9 but no buffer capacity, which means that the medicine may precipitate at pH values below 7 (e.g. glucose injection). Therefore PHARMA-Q FUROSEMIDE INJECTION must not be mixed with any other medicine in the same injection syringe.

6.3 Shelf life

PHARMA-Q FUROSEMIDE INJECTION 20 mg/2 ml: 60 months

PHARMA-Q FUROSEMIDE INJECTION 50 mg/5 ml: 24 months

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light.

6.5 Nature and contents of container

2 ml or 5 ml Amber ampoules packed in boxes of 10.

6.6 Special precautions for disposal and other handling

Opened ampoules should be used immediately and any remainder discarded.

Any unused medicine should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Pharma-Q Holdings (Pty) Ltd

50 Commando Road

Industria West 2003

Johannesburg

South Africa.

8 REGISTRATION NUMBERS

20 mg/2 ml - 32/18.1/0194

50 mg/5 ml - 29/18.1/0664

9 DATE OF FIRST AUTHORISATION

Original date of registration:

PHARMA-Q FUROSEMIDE INJECTION 20 mg/2 ml solution for injection: 12.02.2002

PHARMA-Q FUROSEMIDE INJECTION 50 mg/5 ml solution for injection: 09.04.1996

10 DATE OF REVISION OF THE TEXT

17 April 2015.