AKUMS DRUGS & PHARMACEUTICALS LIMITED
UNOSEMIDE-10 (Furosemide Injection BP 10 mg/ml)
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

UNOSEMIDE-10 (Furosemide Injection BP 10 mg/ml)

1.1 STRENGTH

10 mg/ml

1.2 PHARMACEUTICAL FORM

Injection

2. QUALITY AND QUANTITATIVE COMPOSITION

2.1 QUALITATIVE DECLARATION

Furosemide BP

2.2 QUANTITATIVE DECLARATION

Sr. No.	Ingredients	Specification	Quantity (mg/ml)	Reason for inclusion
1.	Furosemide	BP	10.000	Active
2.	Sodium Chloride	BP	9.000	Tonicity agent
3.	Sodium Hydroxide (Pellets)	BP	10.000	For pH adjustment
4.	Water for Injection	BP	Q.S. to 1 ml	Vehicle

3. PHARMACEUTICAL FORM VISUAL DESCRIPTION:

Injection.

A colourless or almost colourless solution filled in amber colour glass ampoule with white ring on neck.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

When a prompt diuresis is required. Use in emergencies or when oral therapy is precluded.

Indications include:

- Oedema and/or ascites caused by cardiac or hepatic diseases
- Oedema caused by renal diseases (in case of nephrotic syndrome, treatment of the underlying disease is essential)
- Pulmonary oedema (e.g. in case of acute heart failure)
- Hypertensive crisis (in addition to other therapeutic measures)

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Route of administration: Intramuscular or intravenous

General:

The parenteral administration of furosemide is indicated in cases where oral administration is not feasible or not efficient (for example in case of reduced intestinal absorption) or when a quick effect is required. To achieve optimum efficacy and suppress counter-regulation, a continuous furosemide infusion is generally to be preferred to repeated bolus injections. Consideration should be given to current clinical guidelines where available. 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.

Therapy should be individualized according to patient response to gain maximal therapeutic response

and to determine the minimal dose needed to maintain that response.

Adults:

In the absence of conditions requiring a reduced dose (see below) the initial dose recommended for adults and adolescents over 15 years, is of 20 mg to 40 mg furosemide by intravenous (or in exceptional cases intramuscular) administration; the maximum dose varying according to individual response. If larger doses are required, they should be given increasing by 20 mg increments and not given more often than every two hours.

In adults, the recommended maximum daily dose of furosemide administration is 1500 mg.

When administered as an infusion, Furosemide may be administered undiluted using a constant-rate infusion pump, or the solution may be further diluted with a compatible carrier fluid, such as Sodium Chloride Injection B.P. or Ringer's Solution for Injection. In either case, the rate of infusion should not exceed 4mg/minute. The parenteral administration of furosemide is indicated in cases where oral administration is not feasible or not efficient (for example in case of reduced intestinal absorption) or when a quick effect is required. In cases where parenteral administration is used, the switch to oral administration is recommended, as soon as possible.

Children and adolescents (up to 18 years of age):

The experience in children and adolescents are limited. The intravenous administration of furosemide to children and adolescents below 15 years is only recommended in exceptional cases.

The dosage will be adapted to the body weight, and the recommended dose ranges from 0.5 to 1 mg/kg body weight daily up to a maximum total daily dose of 20 mg.

There should be a switch to oral therapy as soon as possible.

Renal impairment:

In patients with severe impairment of renal function (serum creatinine > 5 mg/dl) it is recommended that an infusion rate of 2.5 mg furosemide per minute is not exceeded.

Elderly:

The recommended initial dose is 20 mg/day, increasing gradually until the required response is achieved.

Special dosage recommendations:

For adults, the dose is based on the following conditions:

- Oedema associated to chronic and acute congestive heart failure

The recommended initial dose is 20 to 40 mg daily. This dose can be adapted to the patient´s response, as necessary. The dose should be given in two or three individual doses per day for chronic congestive heart failure and as a bolus for acute congestive heart failure.

- Oedema associated with renal disease

The recommended initial dose is 20 to 40 mg daily. This dose can be adapted to the response as necessary. The total daily dose can be administered as a single dose or as several doses throughout the day. If this does not lead to an optimal fluid excretion increase, furosemide must be administered in continuous intravenous infusion, with an initial rate of 50 mg to 100 mg per hour.

Before beginning the administration of furosemide, hypovolaemia, hypotension and acid-base and electrolytic imbalances must be corrected.

In dialyzed patients, the usual maintenance dose ranges from 250 mg to 1,500 mg daily.

In patients with nephrotic syndrome the dosage must be determined with caution, because of the risk of a higher incidence of adverse events.

- Oedema associated with hepatic disease

When intravenous treatment is absolutely needed, the initial dose should range from 20 mg to 40 mg.

This dose can be adapted to the response as necessary. The total daily dose can be administered as a single dose or in several doses.

Furosemide can be used in combination with aldosterone antagonists in cases in which these agents in monotherapy are not sufficient. In order to avoid complications such as orthostatic intolerance or acid base and electrolytic imbalances or hepatic encephalopathy, the dose must be carefully adjusted to achieve a gradual fluid loss. The dose may produce in adults a daily body weight loss of approximately 0.5 kg. In cases of ascites with oedema, weight loss induced by enhanced diuresis should not exceed 1 kg / day.

- Pulmonary oedema (in acute heart failure)

The initial dose to be administered is 40 mg furosemide by intravenous application. If required by the condition of the patient, another injection of 20 to 40 mg furosemide is given after 30 – 60 minutes.

Furosemide should be used in addition to other therapeutic measures.

- Hypertensive crisis (in addition to other therapeutic measures)

The recommended initial dose in hypertensive crisis is 20 mg to 40 mg administrated in bolus by intravenous injection. This dose can be adapted to the response as necessary.

4.3 METHOD OF ADMINISTRATION

Intravenous furosemide must be injected or infused slowly; a rate of 4 mg per minute must not be exceeded and should never be given in association with other medicinal products in the same syringe. Generally, Furosemide should be administered intravenously. Intramuscular administration must be restricted to exceptional cases where neither oral nor intravenous administration is feasible. It must be noted that intramuscular injection is not suitable for the treatment of acute conditions such as pulmonary oedema.

4.4 CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients.
– Patients with anuria or renal failure with oligoanuria not responding to furosemide
– Renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents
– Renal failure associated with hepatic coma
– Patients with severe hypokalaemia or severe hyponatraemia
– Patients with hypovolaemia (with or without hypotension) or dehydration
– Patients in pre-comatose and comatose state associated with hepatic encephalopathy
– Patients with hypersensitivity to sulphonamides (e.g. Sulfonyureas or antibiotics of sulphonamides group) may show cross-sensitivity to furosemide
– Lactation

4.5 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Careful monitoring is required in case of:

- Patients with partial obstruction of urinary outflow (e.g. prostatic hypertrophy, hydronephrosis, ureterostenosis).

Urinary output must be secured - Patients with hypotension or at increased risk from pronounced fall in blood pressure (patients with coronary artery stenosis or cerebral artery stenosis)

- Patients with manifest or latent diabetes mellitus or variation of glycaemia (regular monitoring of Blood glucose levels necessary)
- Patients with gout and hyperuricaemia (regular monitoring of uric acid levels in serum necessary)
- Patients with hepatic disease or hepatorenal syndrome (renal impairment associated to severe hepatic disease)
- Hypoproteinaemia (associated to nephrotic syndrome, furosemide´s effect may be reduced and its ototoxicity increased)
- Co-administration with lithium salts (monitoring of lithium levels is required, see section 4.5)
- Acute porphyria (the use of diuretics is considered to be unsafe in acute porphyria and caution should be exercised)
- In cases of ascites with oedema, weight loss induced by enhanced diuresis should not exceed 1 kg / day
- Too vigorous diuresis may cause orthostatic hypotension or acute hypotensive episodes.
- NSAIDs may antagonise the diuretic effect of furosemide and other diuretics. Use of NSAIDs with diuretics may increase the risk of nephrotoxicity.
- Where indicated, steps should be taken to correct hypotension or hypovolaemia before commencing therapy.

Cautious dose titration is required:

- Electrolyte variations (e.g. hypokalaemia, hyponatraemia). Potassium supplements and/or dietary measures may be needed to control or avoid hypokalemia
- Fluid variations, dehydration, blood volume reduction with circulatory collapse and possibility of thrombosis and embolism, particular in elderly, with excessive use
- Ototoxicity (if administered faster than 4 mg/min - other ototoxic compounds administered concomitantly can increase this risk
- Administration of high dosages
- Administration in progressive and severe renal disease
- Administration with sorbitol. Concomitant administration of both substances may lead to increased dehydratation (sorbitol might cause additional fluid loss by inducing diarrhoea)
- Administration in Lupus Erythematosus
- Medication that prolong the QT interval

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.

Premature infants (possible development of nephrocalcinosis /nephrolithiasis; renal function must be monitored and renal ultrasonography performed). In premature infants with respiratory distress syndrome, diuretic treatment with furosemide during the first weeks of life can increase the risk of persistent ductus arteriosus Botalli.

Caution should be observed in patients liable to electrolyte deficiency.

Regular monitoring of serum sodium, potassium and creatinine is generally recommended during furosemide therapy; particularly close monitoring is required in patients at high risk of developing electrolyte imbalances or in case of significant additional fluid loss. (e.g. due to vomiting or diarrhoea).

Hypovolaemia or dehydration as well as any significant electrolyte and acid-base disturbances must be corrected.

This may require temporary discontinuation of furosemide.

In patients who are at high risk for radiocontrast nephropathy, furosemide is not recommended to be used for diuresis as part of the preventative measures against radiocontrast-induced nephropathy.

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 cotreatment 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).

Photosensitivity: Cases of photosensitivity reactions have been reported. If photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. If a re-administration is deemed necessary, it is recommended to protect exposed areas to the sun or to artificial UVA.

Furosemide 10 mg/ml Solution for Injection (2ml, 4ml and 5ml ampoule)

This medicinal product contains less than 1 mmol sodium (23 mg) per ampoule i.e. essentially "sodium

free". Furosemide 10 mg/ml Solution for Injection (25 ml vial)

This medicinal product contains approximately 93 mg of sodium per vial. To be taken into consideration by patients on a controlled sodium diet.

4.6 PAEDIATRIC POPULATION

The experience in children and adolescents are limited. The intravenous administration of furosemide to children and adolescents below 15 years is only recommended in exceptional cases.

The dosage will be adapted to the body weight, and the recommended dose ranges from 0.5 to 1 mg/kg body weight daily up to a maximum total daily dose of 20 mg.

There should be a switch to oral therapy as soon as possible.

4.7 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

The concomitant administration of this preparation with cardiac glycosides or hypotensive agents may necessitate adjustment of the dosage of those drugs.

The harmful effects of nephrotoxic drugs on the kidney may be increased**.**

Impairment of renal function may develop in patients receiving treatment with furosemide and high doses of certain cephalosporins.

Oral furosemide and sucralfate must not be taken within 2 hours of each other because sucralfate decreases the absorption of furosemide from the intestine and so reduces its effect.

Corticosteroids, corticotrophin and amphotericin B, also cause potassium loss and severe potassium depletion may occur when administered concurrently with furosemide. Carbenoxolone, liquorice in large amounts, B2 sympathomimetics, prolonged use of laxatives, reboxetine and amphotericin may increase the risk of developing hypokalaemia.

Corticosteroids administered concurrently may cause sodium retention.

If antihypertensive agents, diuretics or other drugs, with blood-pressure-lowering potential are given concomitantly with furosemide, a more pronounced fall in blood pressure must be anticipated.

Concomitant administration of carbamazepine or aminoglutethimide may increase the risk of hyponatraemia.

Furosemide decreases the excretion of lithium salts and may cause increased serum lithium levels, 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 in patients receiving this combination.

Concomitant use of ciclosporine A and furosemide is associated with increased risk of gouty arthritis

secondary to furosemide induced hyperuricaemia and cyclosporine impairment of renal urate excretion. Patients who are at high risk of radiocontrast nephropathy treated with furosemide experienced a higher incidence of deterioration in renal function after receiving radiocontrast compared to high-risk patients who received only intravenous hydration prior to receiving radiocontrast.

Patients who are receiving diuretics may suffer severe hypotension and deterioration in renal function, including cases of renal failure, especially when an angiotensin converting enzyme inhibitor (ACE inhibitor) or angiotensin II receptor antagonist is given for the first time or for the first time in an increased dose. Consideration must be given to interrupting the administration of furosemide temporarily or at least reducing the dose of furosemide for three days before starting treatment with, or increasing the dose of, an ACE inhibitor or angiotensin II receptor antagonist.

Concomitant administration of non-steroidal anti-inflammatory drugs including acetylsalicyclic acid and Indomethacin may reduce the effect of furosemide. In patients with dehydration or hypovolaemia, non-steroidal anti-inflammatory drugs may cause acute renal failure. Salicylate toxicity may be increased by furosemide.

In isolated cases intravenous administration of furosemide within 24 hours of taking chloral hydrate may lead to flushing, sweating attacks, restlessness, nausea, increase in blood pressure and tachycardia. Use of furosemide concomitantly with chloral hydrate is, therefore, not recommended.

Furosemide may potentiate the ototoxicity of aminoglycosides and other ototoxic drugs. Since this may lead to irreversible damage, these drugs must only be used with furosemide if there are compelling medical reasons.

There is a risk of ototoxic effects if cisplatin and furosemide are given concomitantly. In addition, 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.

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).

Attenuation of the effect of furosemide may occur following concurrent administration of phenytoin.

Severe diuresis may occur if metolazone is administered concomitantly.

Probenecid, methotrexate and other drugs which, like furosemide, undergo significant renal tubular secretion may reduce the effect of furosemide. Conversely, furosemide may decrease renal elimination of these drugs. In case of high-dose treatment (in particular, of both furosemide and the other drugs), this may lead to increased serum levels and an increased risk of adverse effects due to furosemide or the concomitant medication.

The effects of antidiabetic drugs and blood pressure increasing sympathomimetics (e.g. epinephrine,

norepinephrine) may be reduced. The effects of curare-type muscle relaxants or of theophylline may be increased.

Risperidone: Caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide should be considered prior to the decision to use (see section 4.4). Levothyroxine: High doses of furosemide may inhibit binding of thyroid hormones to carrier proteins and thereby lead to an initial transient increase in free thyroid hormones, followed by an overall decrease in total thyroid hormone levels. Thyroid hormone levels should be monitored.

4.8 ADDITIONAL INFORMATION ON SPECIAL POPULATIONS

No specific Information

4.9 PAEDIATRIC POPULATION

No specific Information

4.10 FERTILITY, PREGNANCY AND LACTATION

4.10.1 PREGNANCY

Use during pregnancy

Furosemide should not be given during pregnancy unless there are compelling medical reasons. Furosemide crosses the placental barrier, and can therefore cause a diuresis of the fetus. Treatment during pregnancy requires monitoring of fetal growth.

Treatment of pregnancy hypertension and oedema is in general not recommended, as physiological.

Hypovolemia can be induced which causes reduction of placental perfusion.

If use of furosemide is essential for the treatment of cardiac or renal insufficiency during pregnancy,

Careful monitoring of electrolytes, haematocrit and fetal growth is essential. Possible displacement of bilirubin from albumin binding and thus elevated risk of nuclear icterus in hyperbilirubinaemia is discussed for furosemide.

Furosemide can predispose the fetus to hypercalciuria, nephrocalcinosis, and secondary hyperparathyroidism.

Furosemide reaches 100% of the maternal serum concentration in cord blood. No malformations in humans which might be associated with exposure to furosemide have been reported to date. However, there is limited experience to allow a conclusive evaluation of a potential damaging effect in the embryo/fetus.

4.10.2 BREASTFEEDING

Furosemide passes into breast milk and may inhibit lactation. Women must not breast-feed if they are treated with furosemide.

4.10.3 FERTILITY

The safety of furosemide during fertility has not been established.

4.11 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Furosemide 10 mg/ml solution for injection has negligible influence on the ability to drive and use machines. Reduced mental alertness may impair ability to drive or operate dangerous machinery.

4.12 UNDESIRABLE EFFECTS

The frequencies are derived from literature data referring to studies where furosemide is used in a total of 1387 patients, at any dose and in any indication. When the frequency category for the same ADR was different, the highest frequency category was selected.

The following CIOMS frequency rating is used, when applicable:

Very common ≥ 10%; Common ≥ 1 and <10%; Uncommon ≥ 0.1 and <1%; Rare ≥ 0.01 and <0.1%; Very rare <0.01%; Not known (cannot be estimated from available data).

Metabolism and nutrition disorders

Very Common: electrolyte disturbances (including symptomatic) dehydration and hypovolaemia, especially in elderly patients. Blood creatinine increased, blood triglyceride increased.

Common: hyponatremia, hypochloremia, hypokalaemia, blood cholesterol increased. Blood uric acid increased and attacks of gout, urine volume increased.

Uncommon: glucose tolerance impaired.

Not known: hypocalcemia, hypomagnesemia, blood urea increased, metabolic alkalosis, Pseudo-Bartter syndrome.

Vascular Disorders

Very Common: Hypotension including orthostatic hypotension.

Rare: vasculitis.

Not known: thrombosis

Renal and urinary disorders

Common: urine volume increased

Rare: tubulointerstitial nephritis

Not known:

- urine sodium increased, urine chloride increase, urine retention (in patients with a partial obstruction of urinary outflow)

- nephrocalcinosis/nephrolithiasis in premature infants

- renal failure

Gastrointestinal disorders

Uncommon: nausea,

Rare: vomiting, diarrhoea.

Very Rare: pancreatitis acute

Hepatobiliary disorders

Very Rare: cholestasis, transaminases increased

Ear and labyrinth disorders

Uncommon: hearing disorders. Cases of deafness, sometimes irreversible have been reported after oral or IV administration of furosemide.

Very Rare: tinnitus.

Uncommon: deafness (sometimes irreversible)

Skin and subcutaneous tissue disorders

Uncommon: pruritus, urticaria, rashes, dermatitis bullous, erythema multiforme, pemphigoid, dermatitis exfoliative, purpura, photosensitivity reaction

Not known: Stevens-Johnson syndrome, toxic epidermal necrolysis, AGEP (acute generalized exanthematous pustulosis) and DRESS (Drug Rash with Eosinophilia and Systemic Symptoms).

Not Known: acute generalised exanthematous pustulosis (AGEP), lichenoid reactions.

Immune system disorders

Rare: severe anaphylactic or anaphylactoid reactions.

Not known: exacerbation or activation of systemic lupus erythematosus

Nervous system disorders

Rare: paraesthesiae.

Common: hepatic encephalopathy in patients with hepatocellular insufficiency.

Not Known: Dizziness, fainting or loss of consciousness (caused by symptomatic hypotension or by other causes), headache.

Blood and the lymphatic system disorders

Common: haemoconcentration.

Uncommon: thrombocytopenia

Rare: leucopoenia, eosinophilia

Very rare: agranulocytosis, aplastic anaemia, haemolytic anaemia.

Congenital and familiar/genetic disorders

Not known: increased risk of persistence of patent ductus arteriosus when furosemide is administered to premature infants oduring the first weeks of life.

General disorders and administration site conditions

Not known: following intramuscular injection, local reactions such as pain.

Rare: fever.

Musculoskeletal and connective tissue disorders

Not known: cases of rhabdomyolysis have been reported, often in the context of severe hypokalaemia.

4.13 OVERDOSE

The clinical picture in acute or chronic overdose depends primarily on the extent and consequences of electrolyte and fluid loss, e.g. hypovolaemia, dehydration, haemoconcentration, cardiac arrhythmias due to excessive diuresis. Symptoms of these disturbances include severe hypotension (progressing to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion.

Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance. Together with the prevention and treatment of serious complications resulting from such disturbances and of other effects on the body, this corrective action may necessitate general and specific intensive medical monitoring and therapeutic measures.

No specific antidote to furosemide is known. If ingestion has only just taken place, attempts may be made to limit further systemic absorption of the active ingredient by measures such as gastric lavage or those designated to reduce absorption (e.g., activated charcoal).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Diuretic, Sulfonamides, plain

ATC code: CO3C A01

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 Henle with a complex effect on renal circulation. Blood-flow is diverted from the juxta-medullary region to the outer cortex. The principle renal action of Furosemide is to inhibit active chloride transport in the thick ascending limb.

Re-absorption of sodium chloride from the nephron is reduced and a hypotonic or isotonic urine produced. It has been established that prostaglandin (PG) biosynthesis and the renin-angiotensin system are affected by Furosemide administration and that Furosemide alters the renal permeability of the glomerulus to serum proteins.

5.2 PHARMACOKINETIC PROPERTIES

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.

In renal/ hepatic impairment

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

The elderly

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

Newborn

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

5.3 PRECLINICAL SAFETY DATA

Not Applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium Chloride BP

Sodium Hydroxide (Pellets) BP

Water for Injection BP

6.2 INCOMPATIBILITIES

Not Applicable

6.3 SHELF LIFE

36 Months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C. Protect from light and moisture. Do not freeze.

6.5 NATURE AND CONTENTS OF CONTAINER

Tray of 10 x 2 ml ampoules packed in mono carton along with pack insert.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Furosemide 10 mg / ml Solution for Injection may be mixed with neutral and weak alkaline solution with pH between 7 and 10, such as 0.9% sodium chloride and Ringer's lactate solution.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. Product containing visible particles should not be used. For single use only, discard any remaining contents after use.

Furosemide 10 mg / ml Solution for Injection should not be mixed with any other drugs in the injection bottle.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

MARKETING AUTHORISATION HOLDER

Name	:	UNOSOURCE PHARMA LIMITED
Address	:	503-504, 5th Floor, Hubtown Solaris, N.S. Phadke Marg, Andheri (east), Mumbai – 400 069, INDIA
Phone	:	+91-22-61056105
Fax	:	+91-22-61056106

MANUFACTURING SITE ADDRESS

Name: AKUMS DRUGS & PHARMACEUTICALS LTD.

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Phone: 91-0133-4325982

E-mail: inj@akums.in

8. MARKETING AUTHORISATION NUMBER

Not Applicable

9. DATE OF FIRST REGISTRATION

Not Applicable

10. DATE OF REVISION OF TEXT

Not Applicable