

NEW ZEALAND DATA SHEET

1 PRODUCT NAME

UREX FORTE (furosemide 500 mg tablets).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500 mg furosemide.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

UREX FORTE tablets are white round uncoated tablets, one face plain, one face with a break-bar

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Furosemide in a high-dosage formulation such as UREX FORTE (500 mg tablets) is intended exclusively for patients with severely impaired renal function. For use under strict medical supervision only within a hospital setting (see section 4.2 Dose and Method of Administration). High doses of furosemide may be used as an adjuvant treatment of oliguria and in the promotion of diuresis in the treatment of oedema; in selected patients with acute renal failure, e.g. in the post-operative phase and in association with septic infections; in selected patients with chronic renal failure with fluid retention, both in the pre-dialysis phase and when dialysis has become unavoidable, especially in the presence of acute pulmonary oedema; in selected patients with the nephrotic syndrome with severe impairment of renal function e.g. in chronic glomerulonephritis, lupus erythematosus and Kimmelstiel-Wilson syndrome. If diuresis is less than 2.5 L/day dialysis has to be used.

4.2 Dose and method of administration

The high dosage preparation, UREX FORTE tablets, is intended exclusively for administration to patients with greatly reduced glomerular filtration rate. (G.F.R. less than 20 mL/minute but greater than 5 mL/minute). Normal dose may be adequate in patients with greatly reduced G.F.R. mainly if functional oliguria or anuria is observed. Thus, test a normal dose first before administering a high dose.

Before treatment of patients in shock is started, hypovolaemia and hypotension should be dealt with by normal measures. Similarly, disturbed serum electrolytes and acid-base balance should first be corrected.

When treating patients with conditions likely to interfere with micturition, such as prostatic hypertrophy or disturbed consciousness, it is absolutely essential to ensure free urinary drainage. Because of the wide and unpredictable individual variations in responsiveness, it is important to adjust dosage and route of administration to individual needs.

Once the desired rise in urinary output has begun, exact balance of water intake and fluid output must be maintained throughout the course of treatment so as to avoid hypovolaemia or hypotension. Careful electrolyte replacement is also necessary.

The dosage of high strength furosemide, UREX FORTE tablets, given below is for adults only. The dosage regimen for children has not yet been determined. The administration of large doses of furosemide in children has been associated with permanent deafness (see section 4.4 Special Warnings and Precautions for Use). If conventional doses (80 to 160 mg orally) fail to produce an adequate diuresis, an initial dose of 250 mg may be given, increased, if necessary, in steps of

NEW ZEALAND DATA SHEET

250 mg every 4 to 6 hours until adequate diuresis of at least 2.5 L/day is achieved. A maximum daily dose of 1000 mg should not be exceeded.

Paediatric population:

High dose furosemide preparations such as UREX FORTE tablets should not be used in children.

Use in elderly:

No requirement exists for special dosage recommendations in the elderly. However, the smaller peak effect of a single dose together with a delay in its effect in conjunction with reduced renal function, as well as possible need for closer monitoring of water and electrolyte balances in the elderly, must be taken into consideration.

4.3 Contraindications

Known hypersensitivity to furosemide or sulfonamides or to any of the components of Urex. Patients allergic to sulfonamides (e.g. sulfonamide antibiotics or sulfonyleureas) may show cross-sensitivity to Urex.

Anuria or complete renal shutdown. If increasing azotemia and oliguria occur during treatment of severe progressive renal disease discontinue furosemide.

In hepatic coma or precoma and conditions producing electrolyte depletion, furosemide therapy should not be instituted until the underlying condition has been corrected or ameliorated.

Severe hypokalaemia, hyponatraemia, hypovolaemia or hypotension must be regarded as contraindications until serum electrolytes and fluid balance and blood pressure have been restored to normal levels.

In breastfeeding women. (see section 4.6, Fertility, Pregnancy and Lactation - Use in Lactation).

Do not administer furosemide to newborn presenting jaundice or to infants with conditions which might induce hyperbilirubinaemia or kernicterus (Rh incompatibility, familial nonhemolytic jaundice etc.) because of furosemide's "in vitro" potential to displace bilirubin from albumin.

Do not administer furosemide to newborns presenting jaundice or to infants with conditions which might induce hyperbilirubinaemia or kernicterus (e.g. Rhesus incompatibility, familial non-haematolytic jaundice etc.) because of furosemide's in vitro potential to displace bilirubin from albumin.

Normal renal function or impaired renal function with glomerular filtration rates below 5 mL/minute or in excess of 20 mL/minute due to the possibility of severe fluid and electrolyte loss, and renal failure due to poisoning with nephrotoxic or hepatotoxic substances. Hepatic cirrhosis; breast feeding.

4.4 Special warnings and precautions for use

Furosemide is a potent diuretic, which, if given in excessive amounts, can lead to a profound diuresis.

Excessive diuresis may result in dehydration and reduction in blood volume with circulatory collapse and with the possibility of vascular thrombosis and embolism, particularly in elderly patients.

NEW ZEALAND DATA SHEET

Excessive loss of potassium in patients receiving cardiac glycosides may precipitate digitalis toxicity.

In patients with hepatic cirrhosis and ascites, initiation of therapy with furosemide is best carried out in hospital. In hepatic coma or precoma and states of electrolyte depletion, therapy should not be initiated until the basic condition is improved. Sudden alterations of fluid and electrolyte balance in patients with cirrhosis may precipitate hepatic coma, therefore, strict observation is necessary during the period of diuresis. Supplemental potassium chloride and, if required, an aldosterone antagonist are helpful in preventing hypokalaemia and metabolic alkalosis.

Particularly careful monitoring is required in patients with gout, in patients with partial obstruction of urinary outflow, in patients at risk from hypotension (e.g. patients with coronary artery stenosis), in patients with hepatorenal syndrome or in patients with hypoproteinaemia (e.g. associated with nephrotic syndrome). Dose titration, especially in this latter case, is required. In premature infants there is the possible development of nephrocalcinosis/nephrolithiasis and therefore renal function must be monitored and renal ultrasonography must be performed. In premature infants furosemide administered during the first weeks of life may increase the risk of persistence of Botallo's duct.

If increasing azotemia and oliguria occur during treatment of severe progressive renal disease, the drug should be discontinued.

Patients with known sulphonamide sensitivity may show allergic reactions to furosemide.

Cases of tinnitus and reversible or irreversible deafness have been reported. Usually, reports indicate that furosemide ototoxicity is associated with rapid injection, severe renal impairment, doses exceeding several times the usual recommended dose, or concomitant therapy with aminoglycoside antibiotics, ethacrynic acid, or other ototoxic drugs. In patients with hypoproteinaemia e.g. associated with nephrotic syndrome, the effect of Urex may be weakened and its ototoxicity potentiated. Cautious dose titration is required. There have also been some reports of cases, the majority in children undergoing renal transplantation, in which permanent deafness has occurred. In these latter cases, the onset of deafness is usually insidious and gradually progressive up to 6 months after furosemide therapy. Hearing impairment is more likely to occur in patients with severely reduced renal functions who are given large doses of furosemide parenterally, at a rate exceeding 4 mg/min or in patients who are also receiving drugs known to be ototoxic.

Caution should be exercised when administering curare or its derivatives to patients undergoing furosemide therapy and it is advisable to discontinue furosemide for one week prior to any elective surgery.

As with any effective diuretic, electrolyte depletion may occur during therapy with furosemide, especially in patients receiving higher doses and a restricted salt intake. Thus, strict restriction of sodium intake is not advisable in patients receiving furosemide. Periodic determinations of serum electrolytes to detect possible imbalance, should be performed at appropriate intervals, as well as creatinine and blood urea and CO₂ content.

All patients receiving furosemide therapy should be observed for signs of fluid or electrolyte imbalance: namely hyponatraemia, hypochloraemic alkalosis, hypokalaemia, hypomagnesemia or hypocalcaemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs, irrespective of cause, are: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains

NEW ZEALAND DATA SHEET

or cramps, muscular fatigue, hypotension, oliguria, tachycardia, arrhythmia, and gastrointestinal disturbances such as nausea and vomiting. Hypovolaemia or dehydration as well as any significant electrolyte and acid-base disturbances must be corrected, which may require temporary discontinuation of Urex.

Hypokalaemia may develop with furosemide as with any other potent diuretic, especially with brisk diuresis, when cirrhosis is present, during long-term therapy or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalaemia. Digitalis therapy may exaggerate metabolic effects of hypokalaemia, especially with reference to myocardial effects. Caution with potassium is necessary for infants and children; a reduction in dose or discontinuation of furosemide therapy may be necessary.

A potassium rich diet is recommended that will help prevent hypokalaemia, although occasionally potassium supplements or potassium-sparing diuretics may be required, especially in cases of hepatic cirrhosis.

Since rigid sodium restriction is conducive to both hyponatraemia and hypokalaemia, strict restriction in sodium intake is not advisable in patients receiving furosemide.

Asymptomatic hyperuricaemia can occur and rarely, gout may be precipitated.

Periodic checks on urine and blood glucose should be made in diabetics and even those suspected of latent diabetes when receiving furosemide.

Increases in blood glucose and alterations in glucose tolerance tests with abnormalities of the fasting and 2-hour postprandial sugar have been observed, and rare cases of precipitation of diabetes mellitus have been reported.

Furosemide may lower serum calcium levels, and rare cases of tetany have been reported. Accordingly, periodic serum calcium levels should be obtained.

Reversible elevations of blood urea may be seen. These have been observed in association with dehydration, which should be avoided, particularly in patients with renal insufficiency. Transient rises in creatinine levels have also been observed, reflecting a fall in glomerular filtration rate on a haemodynamic basis. There may also be rises in cholesterol and triglyceride levels but these will usually return to normal during long-term treatment with furosemide, within 6 months. It is not clear whether this effect persists long-term.

In patients with prostatic hypertrophy or if disturbances of micturition exist or are suspected, or where consciousness is impaired, care has to be taken for an uninterrupted flow of urine. Symptoms of obstructed urine flow (e.g. in hydronephrosis, or ureteric stenosis) may become manifest or intensified in the course of diuretic therapy.

Renal calcifications (from barely visible on X-ray to staghorn) have occurred in some premature infants treated with intravenous furosemide for oedema due to patent ductus arteriosus (PDA) and hyaline membrane disease. The concurrent use of chlorothiazides has been reported to decrease hypercalciuria and to dissolve some calculi.

The possibility exists of exacerbation or activation of systemic lupus erythematosus.

As with many other drugs, patients should be observed regularly for the possible occurrence of blood dyscrasias, liver or kidney damage, or other idiosyncratic reactions.

Some adverse effects associated with the use of furosemide (e.g. an undesirable pronounced

NEW ZEALAND DATA SHEET

fall in blood pressure) may impair the patients ability to concentrate and react. This constitutes a risk in situations where these abilities are of special importance (e.g. operating a vehicle or machinery).

In premature infants, furosemide administered during the first weeks of life may increase the risk of persistence of Botallo's duct.

In children, urge to defecate, complaints of abdominal pain and cramping have been reported after IV furosemide. An association of these symptoms with a low serum calcium and/or a low calcium/protein ratio is possible.

Particular precautions for UREX FORTE (furosemide 500 mg):

During therapy with high dose UREX FORTE, careful laboratory control is essential and extreme care must always be taken to adjust dosage to individual requirements. Fluid balance and electrolytes should be carefully controlled and, in particular, in patients with shock, measures should be taken to correct blood pressure and blood volume before UREX FORTE therapy.

Paediatric Use:

The use of furosemide in children has been established (refer section 4.2 Dose and Method of Administration for details).

4.5 Interaction with other medicines and other forms of interaction

Interactions with Foods:

The extent to which the absorption of furosemide is affected by taking it with food seems to depend on the pharmaceutical formulation. It is recommended that oral formulations of furosemide, such as Urex, be taken on an empty stomach.

Interactions with Other Drugs:

Combinations that are not recommended:

Concurrent administration of furosemide and aminoglycosides (e.g. kanamycin, gentamicin and tobramycin) may result in an increased incidence of ototoxicity, especially in patients with a decrease in renal function. Except in life-threatening situations, avoid this combination.

It has been reported in the literature that diuretics such as furosemide may enhance the nephrotoxicity of certain antibiotics (e.g. aminoglycosides, cephaloridine, cephalosporin and cephalothin), especially if both are in high doses. The simultaneous administration of these drugs is therefore not advisable.

Anticonvulsants may decrease the response to furosemide. A combination of furosemide and chloral hydrate may lead to diaphoresis, sensation of heat, flushes, tachycardia and elevation of blood pressure. As a result, this combination is not recommended.

Precautions for use:

Furosemide should not be used in combination with ethacrynic acid or cisplatin because of the possibility of ototoxicity. In addition, nephrotoxicity of cisplatin may be enhanced if Urex is not given in sufficiently low doses (e.g. 40 mg in patients with normal renal function) It may also be enhanced with positive fluid balance used to achieve forced diuresis during cisplatin treatment.

Lithium generally should not be given with diuretics because they reduce lithium's renal clearance and add a high risk of lithium toxicity.

NEW ZEALAND DATA SHEET

Simultaneous administration of sucralfate and furosemide may reduce the natriuretic and antihypertensive effects of furosemide. Patients receiving both drugs should be observed closely to determine if the desired diuretic and/or antihypertensive effect of Urex has been achieved. The intake of furosemide and sucralfate should be separated by at least two hours.

The action of other antihypertensive drugs may be potentiated by furosemide; especially in combination with ACE inhibitors. The administration of ACE inhibitors to patients pre-treated with furosemide may lead to a deterioration in renal function or may result in severe hypotension. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs. Therefore consideration must be given to interrupting the administration of Urex temporarily or at least reducing the dose of Urex for 3 days before starting treatment with an ACE inhibitor or increasing its dose.

To be considered:

When a cardiac glycoside is administered concurrently, it should be remembered that potassium or magnesium deficiency increases the sensitivity of the myocardium to digitalis and may increase the toxicity of drugs which induce QT interval prolongation syndrome. When a glucocorticoid is administered during diuretic treatment, the potassium-lowering effect of the steroid should be borne in mind. (See section 4.4 Special Warnings and Precautions for Use). Carbenoxolone, corticosteroids, prolonged use of laxatives or ingestion of liquorice in large amounts may also predispose a patient to hypokalaemia.

Patients receiving high doses of salicylates, as in rheumatic diseases, in conjunction with furosemide may experience salicylate toxicity at lower doses because of competitive renal excretory sites.

Furosemide has been reported to interact with neuromuscular blocking agents. The interaction appears to be dependent on the dose of furosemide and the neuromuscular blocking agent involved. Low doses of furosemide (0.1 to 10µg/kg) enhance the neuromuscular blockade of tubocurarine and succinylcholine. High doses (1-5mg/kg) of furosemide have a tendency to antagonise the skeletal muscle relaxing effect of tubocurarine but may potentiate the action of succinylcholine. The clinical relevance of these findings is uncertain.

Concomitant use of furosemide and amphotericin may result in an excessive potassium loss.

Furosemide may decrease arterial responsiveness to noradrenaline. This diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

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

It has been reported that coadministration of non-steroidal anti-inflammatory drugs (e.g. indomethacin, acetylsalicylic acid) may antagonise the action of furosemide and may cause renal failure in case of preexisting hypovolaemia. Thus, patients receiving both indomethacin and furosemide should be observed closely to determine if the desired diuretic and/or antihypertensive effect of furosemide is achieved. Phenytoin or drugs which undergo significant renal tubular secretion such as methotrexate or probenecid, may attenuate the effects of furosemide. Conversely Urex may decrease renal elimination of these drugs. In the case of high dose treatment (in particular of both Urex and the other drugs), this may lead to an increased risk of adverse effects due to Urex or the concomitant medication.

The effects of curare-type muscle relaxants may be increased.

NEW ZEALAND DATA SHEET

It should be borne in mind that the effect of antidiabetics or of pressor amines (e.g. adrenaline, noradrenaline) may be attenuated by furosemide (see section 4.4 Special Warnings and Precautions for Use).

Non-steroidal anti-inflammatory medicines (e.g. indomethacin, acetylsalicylic acid) may reduce the natriuretic and antihypertensive effects of furosemide in some patients by inhibiting prostaglandin synthesis. NSAIDs may also cause renal failure in case of pre-existing hypovolaemia. Phenytoin or drugs which undergo significant renal tubular secretion such as methotrexate and probenecid, may attenuate the effects of furosemide.

Furosemide was shown to increase the steady state concentration of theophylline by 20% in a small number of asthmatic patients; hence it is appropriate to measure serum theophylline levels when both medicines are given together.

4.6 Fertility, pregnancy and lactation

Use in Pregnancy: Category C

Urex must not be given during pregnancy unless there are compelling medical reasons, such as marked reduction in glomerular filtration. Treatment during pregnancy requires monitoring of foetal growth.

Thiazides, related diuretics and loop diuretics enter the foetal circulation and may cause electrolyte disturbances. Neonatal thrombocytopenia has been reported with thiazides and related diuretics. Loop diuretics like furosemide and bumetanide are probably also associated with this risk. During the latter part of pregnancy products of this type should only be given on sound indications, and then in the lowest effective dose.

Use in Lactation:

The use of furosemide in lactating mothers should be avoided as it passes into the breast milk and may inhibit lactation.

4.7 Effects on ability to drive and use machines

Due to possible hypotension, the patient's ability to drive or operate machinery may be impaired, especially at the commencement of therapy.

4.8 Undesirable effects

Disturbances in electrolytes and water balance may occur during furosemide therapy, especially in patients receiving high doses for a prolonged period.

Excessive diuresis may cause, especially in elderly patients and children, circulatory disturbances such as headache, dizziness, dry mouth or visual impairment because of hypovolaemia. In extreme cases hypovolaemia may lead to dehydration, hypotension, circulatory collapse and in elderly patients in particular, and thrombophilia. Although diuresis occurs rapidly, because of individualised dosage, acute haemodynamic reactions are generally not expected.

Factors such as underlying diseases (liver cirrhosis, cardiac failure), concomitant medication (see section 4.5 Interactions with Other Medicines and Other Forms of Interactions) or nutritional inadequacies (excessive restriction of salt intake) may lead to sodium or other electrolyte or fluid deficiencies. This manifests itself by weakness, a fall in orthostatic blood pressure, dizziness, lethargy, (leg cramps, sweating, bladder spasms, anorexia, vomiting and/or mental confusion (see section 4.4 Special Warnings and Precautions for Use).

NEW ZEALAND DATA SHEET

Furosemide may lower the serum calcium level which may trigger a state of increased neuromuscular irritability. In very rare cases, tetany has been observed. In premature infants, calcium salts may be deposited in the renal tissue (nephrocalcinosis).

Hypomagnesaemia and, in rare cases, tetany or cardiac arrhythmias have been observed as a consequence of increased renal magnesium loss.

Pre-existing metabolic alkalosis (e.g. due to decompensated liver cirrhosis) may be aggravated during furosemide treatment.

Furosemide may cause hypokalaemia, mainly in cases of low potassium diet, vomiting or chronic diarrhoea.

Treatment with Urex may lead to transitory increases in blood creatine and urea levels. Serum levels of uric acid may increase and attacks of gout may occur.

Various forms of dermatitis, including urticaria and rare cases of exfoliative dermatitis and pruritus have occurred. Paresthesias, blurring of vision, postural hypotension, nausea, vomiting and diarrhoea have been reported. Anaemia, leucopenia and thrombocytopenia (with purpura) have occurred, as well as rare cases of agranulocytosis which responded to treatment.

Treatment with furosemide has occasionally caused some deterioration in cases of manifest diabetes, or made latent diabetes manifest.

In addition, the following rare adverse reactions have been reported: sweet taste, oral and gastric burning, paradoxical swelling, headache, jaundice, acute pancreatitis, thrombophlebitis and emboli: however, relationship to the drug has not been definitely established.

Adverse reactions are categorised below by organ system and listed by decreasing severity.

Gastrointestinal System Reactions: Reactions with normal doses of Urex are uncommon. They include; pancreatitis, jaundice (intrahepatic cholestatic jaundice), anorexia, oral and gastric irritation, cramping, diarrhoea, constipation, nausea, vomiting.

Hepatic system: In isolated cases, acute pancreatitis and increases in liver transaminases have been observed. Additionally, intrahepatic chloestasis and jaundice have been reported. Furosemide may increase the bile flow and distend the biliary tree which is already obstructed.

Central Nervous System Reactions: tinnitus and hearing loss, paresthesias, vertigo, dizziness, headache, blurred vision, xanthopsia. Tinnitus, reversible impairment and rarely, permanent tinnitus and impairment of hearing have been observed, especially in patients with markedly reduced renal function or hypoproteinaemia, or in patients who are also receiving drugs known to be ototoxic.

Haematological Reactions: aplastic anaemia (rare), thrombocytopenia, agranulocytosis (rare), leucopenia, anaemia, eosinophilia, thrombophlebitis, haemolytic anaemia.

Dermatologic Hypersensitivity Reactions: necrotising angitis (vasculitis, cutaneous vasculitis), exfoliative dermatitis, erythema multiforme, purpura, urticaria, rash, pruritus and bullous eruptions. Also photosensitivity reactions have been reported.

NEW ZEALAND DATA SHEET

Cardiovascular Reactions: Orthostatic hypotension may occur and be aggravated by, alcohol, barbiturates or narcotics. Ischaemic complications have also been reported in elderly patients.

Urinary System: Excessive diuresis and dehydration could cause transient elevation of serum urea and reduction of GFR. In elderly men with prostatic hypertrophy, acute urinary retention with overflow incontinence may occur. Symptoms of existing conditions of obstructed micturition, such as urethrostenosis or hydronephrosis, may be triggered or aggravated by pronounced diuresis. Interstitial nephritis has also been reported with furosemide use.

Other Reactions: interstitial nephritis, hyperglycaemia, glycosuria, hyperuricemia, fever, transient rise in serum cholesterol and triglyceride, muscle spasm, weakness, restlessness, urinary bladder spasm, thrombophlebitis. Treatment with furosemide has occasionally caused some deterioration in cases of manifest diabetes, or made latent diabetes manifest. Furosemide may lower the serum calcium level (in very rare cases, tetany has been observed). Rarely, fever or paraesthesia and occasionally photosensitivity may occur. In premature infants, calcium salts may be deposited in the renal tissue (nephrocalcinosis/nephrolithiasis). If Urex is administered to premature infants during the first weeks of life, it may increase the risk of persistence of patent ductus arteriosus. Pre-existing metabolic alkalosis (e.g. due to decompensated liver cirrhosis) may be aggravated during furosemide treatment.

Anaphylactic shock is rare, but is acutely life-threatening if it does occur.

Whenever adverse reactions are moderate or severe, furosemide dosage should be reduced or withdrawn.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

The clinical manifestations of acute or chronic overdose depends primarily on the extent and consequences of electrolyte and fluid loss; e.g. dehydration, blood volume reduction, hypotension, electrolyte imbalance, cardiac arrhythmias (including A-V block and ventricular fibrillation), hypokalaemia and hypochloroemic alkalosis, and extensions of the diuretic action of furosemide. Symptoms of these disturbances include severe hypotension (progressing to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion. In cirrhotic patients, overdosage may precipitate hepatic coma.

The acute toxicity of furosemide has been determined in mice, rats and dogs. In all three, the oral LD₅₀ exceeded 1000 mg/kg body weight. The acute intragastric toxicity in neonatal rats is 7 to 10 times that of adult rats. The concentration of furosemide in biological fluids associated with death is not known.

Treatment of overdosage:

No specific antidote to Urex 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 designed to reduce absorption (e.g. activated charcoal).

Treatment of overdosage is supportive. Discontinue the drug. Institute water and electrolyte replacements immediately and adjust in accordance with urine output. Haemodialysis does not accelerate furosemide elimination. Serum electrolytes, carbon dioxide level and blood pressure

NEW ZEALAND DATA SHEET

should be determined frequently. Adequate drainage must be assured in patients with urinary bladder obstruction (such as prostatic hypertrophy)
{For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).}

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Diuretics

ATC code: C03CA01

Furosemide is a potent diuretic. It inhibits sodium reabsorption in the ascending limb of Henle's loop and in both the proximal and distal tubules. The action on the distal tubule is independent of any inhibitory effect on carbonic anhydrase or aldosterone. The high degree of efficacy is due to this unique site of action.

Furosemide may promote diuresis in cases which have previously proved resistant to other diuretics.

5.2 Pharmacokinetic properties

Absorption

Furosemide has no significant pharmacological effects other than on renal function. Furosemide is rapidly absorbed from the upper gastrointestinal tract.

Absorption rates in healthy subjects have been reported from 60-69%; 45% in patients with end stage renal failure; and 34-80 in patients with congestive heart failure. Bioavailability in healthy subjects is 60-69%.

Distribution

The mean apparent volume of distribution in the steady state ranges from 0.07 to 0.18 L/kg body weight in healthy subjects.

Biotransformation

Recent evidence suggests that furosemide glucuronide is the only or at least the major biotransformation product of furosemide in man. Furosemide is extensively bound to plasma proteins, mainly to albumin. Plasma concentrations ranging from 1 to 400 µg/mL are 91 to 99% bound in healthy individuals.

The unbound fraction averages 2.3 to 4.1% of therapeutic concentrations.

Excretion

Furosemide's diuretic effect is apparent within 1 hour following oral administration and the peak effect occurs in the first or second hour. The duration of action is 4 to 5 hours but may continue up to 8 hours.

At the peak of diuretic response 30 to 40% of the filtered sodium load may be excreted, along with some potassium and with chloride as the major anion. Furosemide augments the potassium output as a result of increased distal potassium secretion. Its diuretic action is independent of changes in acid-base balance. Under conditions of acidosis or alkalosis the diuretic produces a chloruresis without augmentation of bicarbonate excretion.

Urinary excretion is accomplished both by glomerular filtration and proximal tubular secretion which accounts for roughly 66% of the ingested dose, the remainder being excreted in the

NEW ZEALAND DATA SHEET

faeces. A small fraction is metabolised.

The following table summarises furosemide's elimination kinetics in both normal subjects and patients with renal insufficiency:

Subjects	Administration Route	Dose (mg)	Administration Rate	Biliary Excretion	Max. Serum Conc.	t _{1/2} hr.
Normal	Oral	40	-	10 to 15%	<1 µg/mL	4.0
Normal	I.V.	40	bolus	10 to 15%	2.5 µg/mL	4.5
Renal insufficiency	I.V.	1000	25 mg/min	60%	53 µg/mL	13.5
Renal insufficiency	I.V.	1000	4 mg/min	-	29 µg/mL	-

Furosemide administration may induce extracellular metabolic alkalosis, primarily by virtue of the disproportionate loss of chloride but also, in part, as a result of the variable depletion of potassium.

5.3 Preclinical safety data

Data not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Urex Forte contains: lactose monohydrate, maize starch, colloidal anhydrous silica, magnesium stearate and maltodextrin.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 Years

6.4 Special precautions for storage

Store below 30°C. Protect from light

6.5 Nature and contents of container

Urex Forte: 50's in blister pack (PVC/PVDC-Al)

6.6 Special precautions for disposal

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

NEW ZEALAND DATA SHEET

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Pharmacy Retailing (NZ) Limited trading as Healthcare Logistics 58
Richard Pearse Drive
Airport Oaks Mangere
AUCKLAND

9 DATE OF FIRST APPROVAL

7 June 2013

10 DATE OF REVISION OF THE TEXT

13 May 2019

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
all	Reformat and update active name to furosemide