SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:

UNOSEMIDE-10 (Furosemide Injection BP)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each ml contains:
Furosemide BP……..... 10 mg
Water for Injections BP…...… q.s.

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM:

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

4. CLINICAL PARTICULARS:

4.1. Therapeutic Indications:

The intravenous formulation is appropriate for use in emergencies or when oral therapy is precluded. Indications include cardiac, pulmonary, hepatic and renal oedema.

4.2. Posology And Method Of Administration:

Route of administration: Intramuscular or intravenous
Intravenous furosemide may be injected or infused slowly; a rate of 4 mg per minute must not be exceeded.
Intramuscular administration must be restricted to exceptional cases where neither oral or nor intravenous administration are feasible.
Doses of 20 to 50 mg intramuscularly or intravenously may be given initially. If larger doses are required, they should be given increasing by 20 mg increments and not given more often than every two hours. If doses greater than 50mg are required, it is recommended maximum daily dose of furosemide administration is 1500 mg.

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

Children:
Parenteral doses for children range from 0.5 to 1.5 mg/kg body weight daily up to a maximum total daily dose of 20 mg.

4.3. Contraindications:

Furosemide is contraindicated in patients with anuria and in patients with a history of hypersensitivity to furosemide.

4.4. Special Warnings And Precautions For Use:

In patient with hepatic cirrhosis and ascites, furosemide therapy is best initiated in hospital.
In hepatic coma and in states of electrolyte depletion, therapy should not be instituted 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 period of diuresis. Supplemental potassium chloride and, if required an aldosterone antagonist are helpful in preventing hypokalemia and metabolic alkalosis.

If increasing azotemia and oliguria occur during treatment of severe progressive renal disease, furosemide should be discontinued. Cases of tinnitus and reversible and irreversible hearing impairment and deafness have been reported. Reports usually indicate that furosemide ototoxicity is associated with rapid injection, severe renal impairment, the use of higher than recommended doses, hypoproteinemia, or concomitant therapy with amino glycoside antibiotics, ethacrynic acid, or other ototoxic drugs.
Hearing loss in neonates has been associated with the use of furosemide injection. Excessive diuresis may cause dehydration and blood volume reduction with circulatory collapse and possibly vascular thrombosis and embolism, particularly in elderly patients.
As with any effective diuretic, electrolyte depletion may occur during furosemide therapy, especially in patients receiving higher doses and a restricted salt intake. Hypokalaemia may develop with furosemide, especially with brisk diuresis, inadequate oral electrolyte intake, when cirrhosis is present, or during concomitant use of corticosteroids, ACTH, liquorice in large amounts or prolonged use of laxatives. Digitalis therapy may exaggerate metabolic effect of hypokalaemia, especially myocardial effects.
All patients receiving furosemide therapy should be observed for these signs or symptoms of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, hypokalaemia, hypomagnesaemia or hypocalcemia): dryness of mouth, thirst weakness, lethargy, drowsiness, restlessness, muscle pain or cramps, muscular fatigue, hypotension, oliguria, tachycardia, arrhythmia or gastrointestinal disturbances such as nausea and vomiting.
In patient at high risk for radiocontrast nephropathy, furosemide can lead to 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. In patients with hypoproteinemia (e.g. associated with nephrotic syndrome) the effect of furosemide may be weakened and its ototoxicity potentiated.
Asymptomatic hyperuricemia can occur and gout may rarely be precipitated.

4.5. Interation with other medicinal products and other forms of interactions:

Furosemide may increase the ototoxic potential of aminoglycoside antibiotics, especially in the presence of impaired renal function. Except in life threatening situations, avoid the combination. Furosemide should not be used concomitantly with ethacrynic acid because of the possibility of ototoxicity. Patients receiving high doses of salicylates concomitantly with furosemide, as in rheumatic disease, may experience salicylate toxicity at lower doses because of competitive renal excretory sites.
There is a risk of ototoxic effects if cisplatin and furosemide are given concomitantly. In addition, nephrotoxicity of nephrotoxic drugs such as cisplatin may be enhanced if furosemide is not given in lower doses and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.

Furosemide has a tendency to antagonize the skeletal muscle relaxing effect of tubocurarine and may potentiate the action of Succinylcholine.

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

Furosemide combined with angiotensin converting enzyme inhibitors or angiotensin II receptor blockers may lead to severe hypotension and deterioration in renal function, including renal failure. An interruption or reduction in the dosage of furosemide, angiotensin converting enzyme inhibitors, or angiotensin receptor blockers may be necessary.

Furosemide may add to or potentiate the therapeutic effect of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Furosemide may decrease arterial responsiveness to norepinephrine. However, norepinephrine may still be used effectively.

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.

Phenytoin interferes directly with renal action of furosemide.

Methotrexate or other drugs that, like furosemide, undergo significant renal tubular secretion may reduce the effect of furosemide. Conversely, furosemide may decrease renal elimination of other drugs that undergo tubular secretion. High dose treatment of both furosemide and these other drugs may result in elevated serum levels of these drugs and may potentiate their toxicity as well as the toxicity of furosemide.

Furosemide can increase the risk of cephalosporin-induced nephrotoxicity even in the setting of minor or transient renal impairment. Concomitant use of cyclosporine and furosemide is associated with increased risk of gouty arthritis secondary to furosemide induced hyperuricemia and cyclosporine impairment of renal urate excretion.

4.6. Pregnancy and Lactation:

Pregnancy

Furosemide has been shown to cause unexplained maternal deaths and absorption in rabbits at 2, 4 and 8 times the maximal recommended human oral dose. There are no adequate and well-controlled studies in pregnant women. Furosemide should be used during pregnancy only if the potential benefits justifies the potential risk to the foetus. Treatment during pregnancy requires monitoring of fetal growth because of the potential for higher fetal birth weights.

The results of the mouse study and one of the three rabbit studies also showed an increased incidence and severity of hydronephrosis (distention of the renal pelvis and, in cases, of the ureters) in fetuses derived from treated dams as compared with the incidence of foetuses from the control group.

Lactation

Because it appears in breast milk, caution should be exercised when furosemide is administered to a nursing mother.

4.7. Effects on ability to drive and use machine:

Reduced mental alertness may impair ability to drive or operate dangerous machinery.

4.8. Undesirable effects:

Thrombocytopenia, Leucopenia, Aplastic anaemia, Paraesthesia, Hepatic encephalopathy, Nephrocalcinosis, Headache, Dizziness, Drowsiness, Weakness, Disorders of vision, Dry mouth, Orthostatic intolerance.

4.9. Overdosage:

The principal signs and symptoms of overdose with furosemide are dehydration, blood volume reduction, hypotension, electrolyte imbalance, hypokalaemia and hypochloremic alkalosis, and are extensions of its diuretic action.

The acute toxicity of furosemide has been determined in mice, rat and dogs. In all three, the oral LD50 exceeded 1000 mg/kg body weight, while the intravenous LD50 ranged from 300 to 680 mg/kg. 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 toxicity or death is not known.

Treatment of Overdosage is supportive and consists of replacement of excessive fluid and electrolyte losses. Serum electrolytes, carbon dioxide level and blood pressure should be determined frequently. Adequate drainage must be assured in patients with urinary bladder outlet obstruction (such as prostatic hypertrophy). Hemodialysis does not accelerate furosemide elimination.

5. PHARMACOLOGICAL PROPERTIES:

5.1. Pharmacodynamics Properties:

Furosemide, loop diuretic, inhibits water reabsorption in the nephron by blocking the sodium- potassium-chloride cotransporter (NKCC2) in the thick ascending limb of the loop of Henle. This is achieved through competitive inhibition at the chloride binding site on the cotransporter, thus preventing the transport of sodium from the lumen of the loop of Henle into basolateral interstitium.

5.2. Pharmacokinetic Properties:

Furosemide is weak carboxylic acid which exist 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. 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 bound to plasma albumin and little biotransformation takes place.

Furosemide is mainly eliminated via the kidney (80-90%); a small fraction of the dose undergoes biliary elimination and 10-15% of the activity can be recovered from the faeces.

5.3. Preclinical Safety Data:

Non-clinical data reveal no special hazard for humans based on repeated dose toxicity, genotoxicity and carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS:

6.1. list of Excipients:

Di-sodium Edetate BP, Sodium Hydroxide BP (Pellets), Hydrochloric Acid BP, Water for Injections BP.

6.2. Incompatibilities:

Furosemide should not be mixed with strong acid solution (pH lower than 5.5), such as solutions containing ascorbic acid, noradrenaline and adrenaline, due to the risk of precipitation. This medical product should not be mixed with other medicinal products.

6.3. Shelf Life:
36 Months

6.4. Special Precautions for Storage:
Store below 30ºC. Protect from light & moisture. Do not freeze.

6.5. Nature and contents of Container:
Tray of 10 x 2 ml ampoules packed in monocarton along with pack insert.

6.6. Special Precaution for Disposal:
No special requirement.

7. MARKETING AUTHORIZATION HOLDER:
Unosource Pharma Ltd.
503-504, 5th Floor Hubtown Solaris
N.S. Phadke Marg, Andheri (East) MumbaI-400069, India

8. MARKETING AUTHORISATION NUMBER(S):
05247/5402/NMR/2017

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION:
07-08-2020

10. DATE OF REVISION OF THE TEXT:
07-07-2023