Interactions
The interactions of furosemide that are due to its effects on fluid and electrolyte balance are similar to those of hydrochlorothiazide. Furosemide may enhance the nephrotoxicity of cephalosporin antibacterials such as cefalotin and can enhance the ototoxicity of aminoglycoside antibacterials and other ototoxic drugs.

Precautions
Precautions and contra-indications for furosemide that are dependent on its effects on fluid and electrolyte balance are similar to those of the thiazide diuretics. Although furosemide is used in high doses for oliguria due to chronic or acute renal impairment it should not be given in anuria or in renal failure caused by nephrotoxic or hepatotoxic drugs nor in renal failure associated with hepatic coma. Furosemide should not be given in pre-comatose states associated with hepatic cirrhosis. It should be used with care in patients with prostatic hyperplasia or impairment of micturition since it can precipitate acute urinary retention. To reduce the risk of ototoxicity, licensed product information recommends that furosemide should not be injected intravenously at a rate exceeding 4 mg/minute although the *BNF* advises that a single dose of up to 80 mg may be given more rapidly. Furosemide should be used with caution during pregnancy and breast feeding since it crosses the placenta and also appears in breast milk. Furosemide may compromise placental perfusion by reducing maternal blood volume; it may also inhibit lactation.

Adverse Effects and Precautions
Most adverse effects of furosemide occur with high doses, and serious effects are uncommon. The most common adverse effect is fluid and electrolyte imbalance including hyponatraemia, hypokalaemia, and hypochloraemic alkalosis, particularly after large doses or prolonged use. Signs of electrolyte imbalance include headache, hypotension, muscle cramps, dry mouth, thirst, weakness, lethargy, drowsiness, restlessness, oliguria, cardiac arrhythmias, and gastrointestinal disturbances. Hypovolaemia and dehydration may occur, especially in the elderly. Because of their shorter duration of action, the risk of hypokalaemia may be less with loop diuretics such as furosemide than with thiazide diuretics. Unlike the thiazides, furosemide increases the urinary excretion of calcium and nephrocalcinosis has been reported in preterm infants. Furosemide may cause hyperuricaemia and precipitate gout in some patients. It may provoke hyperglycaemia and glycosuria, but probably to a lesser extent than the thiazide diuretics. Pancreatitis and cholestatic jaundice seem to occur more often than with the thiazides. Other adverse effects include blurred vision, yellow vision, dizziness, headache, and orthostatic hypotension. Other adverse effects occur rarely. Skin rashes and photosensitivity reactions may be severe; hypersensitivity reactions include interstitial nephritis and vasculitis; fever has also been reported. Bone marrow depression may occur: there have been reports of agranulocytosis, thrombocytopenia, and leucopenia. Tinnitus and deafness may occur, in particular during rapid high-dose parenteral furosemide. Deafness may be permanent, especially in patients taking other ototoxic drugs

WARNINGS
In patients with hepatic cirrhosis and ascites, furosemide therapy is best initiated in the 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 the 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 or 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 aminoglycoside antibiotics, ethacrynic acid, or other ototoxic drugs. If the physician elects to use high dose parenteral therapy, controlled intravenous infusion is advisable (for adults, an infusion rate not exceeding 4 mg furosemide per minute has been used).

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

Pregnancy
Teratogenic Effects: Pregnancy Category C. Furosemide has been shown to cause unexplained maternal deaths and abortions 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 benefit justifies the potential risk to the fetus. Treatment during pregnancy requires monitoring of fetal growth because of the potential for higher fetal birth weights. The effects of furosemide on embryonic and fetal development and on pregnant dams were studied in mice, rats and rabbits. Furosemide caused unexplained maternal deaths and abortions in the rabbit at the lowest dose of 25 mg/kg (2 times the maximal recommended human oral dose of 600 mg/day). In another study, a dose of 50 mg/kg (4 times the maximal recommended human oral dose of 600 mg/day) also caused maternal deaths and abortions when administered to rabbits between Days 12 and 17 of gestation. In a third study, none of the pregnant rabbits survived an oral dose of 100 mg/kg. Data from the above studies indicate fetal lethality that can precede maternal deaths. 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 some cases, of the ureters) in fetuses derived from the treated dams as compared with the incidence of fetuses from the control group.

Nursing Mothers:
Because it appears in breast milk, caution should be exercised when furosemide is administered to a nursing mother. Furosemide may inhibit lactation.

Storage: -Store Protected from Light, & temperature not exceeding 25° C.
Do not allow to freeze.
Improper Storage may deteriorate the product
Keep medicine out of reach of children.
Presentation:- 5x2 ml Ampoule pack blister & 10 blister pack in a outer carton

Manufactured by:
AMERICAN REMEDIES ©
Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
(An ISO 9001-2015 Certified Company)
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For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

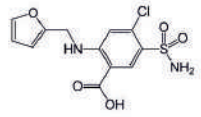
℞ Furosemide Injection IP

AMERICAN
Frasix 20 20mg/2ml

FOR IM/IV USE ONLY
Composition:-
Each ml Contains:-

Furosemide	IP	10 mg
Water for Injection	IP	q.s

Description
Furosemide is a diuretic which is an anthranilic acid derivative. Chemically, it is 4-chloroNfurfuryl 5-sulfamoylanthranilic acid. Furosemide Injection 10 mg/mL is a sterile, non-pyrogenic solution in ampoules for intravenous and intramuscular injection. Furosemide is a white to off-white odourless crystalline powder. It is practically insoluble in water, sparingly soluble in alcohol, freely soluble in dilute alkali solutions and insoluble in dilute acids. The molecular formula is $C_{12}H_{11}ClN_2O_5S$ and molecular weight is 330.74, the structural formula is as follows:



Furosemide

PHARMACOLOGY
Pharmacokinetics
Furosemide is fairly rapidly absorbed from the gastrointestinal tract; bioavailability has been reported to be about 60 to 70% but absorption is variable and erratic. The half-life of furosemide is up to about 2 hours although it is prolonged in neonates and in patients with renal and hepatic impairment. Furosemide is up to 99% bound to plasma albumin, and is mainly excreted in the urine, largely unchanged. There is also some excretion via the bile and non-renal elimination is considerably increased in renal impairment. Furosemide crosses the placental barrier and is distributed into breast milk. The clearance of furosemide is not increased by haemodialysis.

Uses and Administration
Furosemide is a potent diuretic with a rapid action. Like the other loop or high-ceiling diuretics it is used in the treatment of oedema associated with heart failure (below), including pulmonary oedema, and with renal and hepatic disorders (but see Precautions, above) and may be effective in patients unresponsive to thiazide diuretics. It is also used in high doses in the management of oliguria due to renal failure or insufficiency. Furosemide is also used in the treatment of hypertension, either alone or with other antihypertensives. Furosemide inhibits the reabsorption of electrolytes primarily in the thick ascending limb of the loop of Henle and also in the distal renal tubules. It may also have a direct effect in the proximal tubules. Excretion of sodium, potassium, calcium, and chloride ions is increased and water excretion enhanced. It has no clinically significant effect on carbonic anhydrase. See Action, below, for further reference to its mechanism of action.

Administration and dosage.
Furosemide's effects are evident within 30 minutes to 1 hour after an oral dose, peak at 1 to 2 hours, and last for about 4 to 6 hours; after intravenous injection its effects are evident in about 5 minutes and last for about 2 hours. It is given orally, usually in the morning. Alternatively it may be given intramuscularly or intravenously as the sodium salt; doses are expressed in terms of furosemide base. Licensed product information recommends that whether by direct intravenous injection or by infusion the rate of intravenous dosage should not exceed 4 mg/minute although the *BNF* advises that a single dose of up to 80 mg may be given more rapidly. Unlike the thiazide diuretics where, owing to their flat dose-response curve, very little is gained by increasing the dose, furosemide has a steep dose-response curve, which gives it a wide therapeutic range. In the treatment of **oedema**, the usual initial oral dose is 40 mg once daily, adjusted as necessary according to response. Mild cases may respond to 20 mg daily or 40 mg on alternate days. Some patients may need doses of 80 mg or more daily given as one or two doses daily, or intermittently. Severe cases may require gradual titration of the furosemide dosage up to 600 mg daily. In an emergency or when oral therapy cannot be given, 20 to 50 mg of furosemide may be given by slow intravenous injection; intramuscular injection may be given in exceptional cases but is not suitable for acute conditions. If necessary further doses may be given, increasing by 20-mg increments and not given more often than every 2 hours. If doses above 50 mg are required they should be given by slow intravenous infusion. For pulmonary oedema, if an initial slow intravenous injection of 40 mg does not produce a satisfactory response within one hour, a further 80 mg may be given slowly intravenously. For children, the usual oral dose is 1 to 3 mg/kg daily up to a maximum of 40 mg daily; doses by injection are 0.5 to 1.5 mg/kg daily up to a maximum of 20 mg daily.

High-dose therapy.
In the management of **oliguria** in acute or chronic renal failure where the glomerular filtration rate is less than 20 mL/minute but greater than 5 mL/minute, furosemide 250 mg diluted to 250 mL in a suitable diluent is infused over one hour. If urine output is insufficient within the next hour, this dose may be followed by 500 mg added to an appropriate infusion fluid, the total volume of which must be governed by the patient's state of hydration, and infused over about 2 hours. If a satisfactory urine output has still not been achieved within one hour of the end of the second infusion then a third dose of 1 g may be infused over about 4 hours. The rate of infusion should never exceed 4 mg/minute. In oliguric patients with significant fluid overload, the injection may be given without dilution directly into the vein, using a constant rate infusion pump with a micrometer screw-gauge adjustment; the rate should still never exceed 4 mg/minute. Patients who do not respond to a dose of 1 g probably require dialysis. If the response to either dosage method is satisfactory, the effective dose (of up to 1 g) may then be repeated every 24 hours. Dosage adjustments should subsequently be made according to the patient's response.
Alternatively, oral treatment may be maintained; 500 mg should be given orally for each 250 mg required by injection. When used in chronic renal impairment, an initial oral dose of 250 mg may be given, increased, if necessary in steps of 250 mg every 4 to 6 hours to a maximum of 1.5 g in 24 hours; in exceptional cases up to 2 g in 24 hours may be given. Dosage adjustments should subsequently be made according to the patient's response.
During treatment with these high-dose forms of furosemide therapy, careful laboratory control is essential. Fluid balance and electrolytes should be carefully controlled and, in particular, in patients with shock, measures should be taken to correct the blood pressure and circulating blood volume, before commencing this type of treatment. High-dose furosemide therapy is contra-indicated in renal failure caused by nephrotoxic or hepatotoxic drugs, and in renal failure associated with hepatic coma.