Furosemide (Frusemide)

Newborn use only

2018

<table>
<tr><td>Alert</td><td></td></tr>
<tr><td>Indication</td><td>Heart failure.
Fluid overload.
Short-term treatment in infants with or developing chronic lung disease.
Oliguric renal failure.
Diuresis renography.</td></tr>
<tr><td>Action</td><td>Potent loop diuretic. Inhibits sodium and chloride absorption in the ascending limb of the loop of Henle and in the proximal and the distal tubules.
Furosemide causes urinary losses of water, sodium (increases fractional excretion of sodium by 20–25%),[2] potassium and chloride. Urinary losses of calcium and magnesium and urinary pH are increased.</td></tr>
<tr><td>Drug Type</td><td>Loop diuretic.</td></tr>
<tr><td>Trade Name</td><td>IV: Furosemide Sandoz Injection, Furosemide-Claris, Lasix High Dose Concentrate, Lasix Solution. [Excipients: Sodium hydroxide, sodium chloride and water for injection].

Oral: Lasix oral solution. Note: Contains 12.7% v/v alcohol. [Other Excipients: Sorbitol, glycerol, sodium hydroxide, methyl hydroxybenzoate, propyl hydroxybenzoate, quinoline yellow, sunset yellow FCF, orange flavour, purified water]</td></tr>
<tr><td>Presentation</td><td>IV: 20 mg/2 mL, 40 mg/4 mL or 250 mg/25 mL
Oral: 10 mg/mL, 30 mL
Note: Commercial preparation “Lasix” contains 12.7% v/v alcohol.
Non-alcohol containing suspension can be compounded by local pharmacy.</td></tr>
<tr><td>Dosage / Interval</td><td>IV or PO*: 1 to 2 mg/kg/dose. Dose interval as follows:
<table>
<tr><td>Corrected gestational age/Postmenstrual age</td><td>Interval</td></tr>
<tr><td>Preterm infant ≤ 33 weeks</td><td>Every 24 hours</td></tr>
<tr><td>Preterm infant > 33 weeks</td><td>12–24 hours</td></tr>
<tr><td>Term infant 0–30 days</td><td>Every 12 hours</td></tr>
<tr><td>Term infant > 30 days</td><td>8–12 hours</td></tr>
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*PO: Dose may be increased up to maximum 6 mg/kg/dose in term infants with heart failure.

IV Infusion: 0.05 to 0.2 mg/kg/hour increased to maximum 0.4 mg/kg/hour if urine output < 1 mL/kg/hour.

Diuresis renography: 1 mg/kg stat.</td></tr>
<tr><td>Maximum dose</td><td>IV: 2 mg/kg/dose
IV infusion: 0.4 mg/kg/hour
Oral: 6 mg/kg/dose</td></tr>
<tr><td>Route</td><td>IV or oral</td></tr>
<tr><td>Preparation/Dilution</td><td>IV bolus: Give undiluted. If dilution required draw up 0.5mL (5 mg of furosemide) and add 9.5mL sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 0.5 mg/mL.

IV infusion:
Single-strength infusion: Draw up 0.5 mL/kg (5 mg/kg of furosemide) and make up to 10 mL with sodium chloride 0.9% or glucose 5% or glucose 10% or glucose 20% to make a 0.5 mg/kg/mL solution. Infusing at a rate of 0.1 mL/hour = 0.05 mg/kg/hour.

Double-strength infusion: Draw up 1 mL/kg (10 mg/kg of furosemide) and make up to 10 mL with sodium chloride 0.9% or glucose 5% or glucose 10% or glucose 20% to make a 1 mg/kg/mL solution. Infusing at a rate of 0.1 mL/hour = 0.1 mg/kg/hour.

Oral: Use as supplied undiluted.</td></tr>
</table>

Administration	IV bolus over 2–4 minutes: maximum rate not to exceed 0.5 mg/kg/minute or 4 mg/minute. For diuresis renography – dose should be given as a push.[1] IV infusion: Via syringe pump Oral: Solution may be administered without regard to feeds.
Monitoring	Urine output, weight, serum sodium and potassium. Screening for nephrocalcinosis may be required for preterm infants on prolonged therapy.
Contraindications	Known hypersensitivity to furosemide. Severe hypokalaemia, hyponatraemia, hypovolaemia, dehydration or hypotension must be regarded as contraindications until serum electrolytes, fluid balance and blood pressure have been restored to normal levels. Severe jaundice at risk of bilirubin encephalopathy.
Precautions	Commercially available oral furosemide solution contains ethanol and 2 mg/kg/day of solution equates to 1.4 mL/kg/week ethanol intake [equivalent to 1 unit alcohol/week for a man weighing 70 kg]. If increasing azotaemia and oliguria occur during treatment of severe progressive renal disease, discontinue furosemide. Jaundice – furosemide may displace bilirubin from albumin. However, bilirubin displacement is negligible with standard doses.
Drug Interactions	Furosemide can cause the depletion of potassium and magnesium, which can predispose patients to serious cardiac arrhythmias, particularly in the presence of digitalis therapy. The risk of electrolyte depletion is markedly enhanced when 2 diuretics are used in combination. May prolong action of muscle relaxants. Avoid concomitant usage of aminoglycosides to avoid ototoxicity.
Adverse Reactions	Furosemide is associated with renal losses of calcium, sodium, chloride and potassium. Prolonged and higher doses of furosemide are associated with ototoxicity and nephrocalcinosis.
Compatibility	Fluids: Glucose 5%, glucose 10%, glucose 20%, sodium chloride 0.9% Y-site: Amifostine, amikacin, anidulafungin, aztreonam, bivalirudin, ceftaroline fosamil, dexmedetomidine, doripenem, foscarnet, granisetron, heparin sodium, hydrocortisone sodium succinate, levosimendan, linezolid, lorazepam, metoprolol, piperacillin-tazobactam (EDTA-free), potassium chloride, remifentanil, sodium nitroprusside, tirofiban, tobramycin.
Incompatibility	Fluids: No information. Variable compatibility with parenteral nutrition solutions. Y-site: Atracurium, azithromycin, benztropine, buprenorphine, caffeine citrate, caspofungin, chlorpromazine, ciprofloxacin, dolasetron, droperidol, eptifibatide, erythromycin, esmolol, filgrastim, fluconazole, gentamicin, glycopyrrolate, haloperidol lactate, hyaluronidase, hydralazine, ketamine, labetalol, metaraminol, metoclopramide, midazolam, milrinone, moxifloxacin, mycophenolate mofetil, ondansetron, pancuronium, pentamidine, pethidine, phentolamine, phenylephrine, promethazine, protamine, quinine, rocuronium, vancomycin, vasopressin, vecuronium, verapamil.
Stability	Do not use if solution is discoloured. Diluted IV solution: Stable for 24 hours at 2−25°C (preferred storage is 2-8°C). Oral solution: Commercial preparation “Lasix”- Discard 8 weeks after opening. Compounded suspension – 14 day expiry.
Storage	Vial: Store below 25°C. Protect from light. Occasionally crystal deposits may be seen when ampoules are stored at low temperatures. Dissolve crystals by warming to 40°C and injection may be used. Discard solutions that are yellow. Oral solution:

	Commercial preparation - store below 25°C Compounded suspension – refrigerated at 2-8°C
Special Comments	Loop diuretics are preferred for initial treatment of heart failure as they have a greater effect on sodium excretion compared to distal diuretics.[2] Potassium deficits can be corrected by the short-term use of potassium supplements. Concomitant administration of a potassium-retaining agent such as spironolactone can prevent potassium depletion in most infants taking a loop diuretic. Alternate day dosing may be considered to reduce the risk of electrolyte and mineral abnormalities. Plasma $t_{½}$ of furosemide is 7.7–26.8 hours in neonates. It is longer in immature infants (mean $t_{½}$ > 20 hours).[22] The $t_{½}$ is prolonged by renal and hepatic insufficiency. Blood concentrations exceeding 0.05 mg/mL may be associated with ototoxicity.
Evidence summary	**Efficacy:** **Heart failure:** Controlled trials have demonstrated diuretics increase urinary sodium excretion and decrease physical signs of fluid retention in patients with HF. In short-term studies, diuretic therapy led to a reduction in jugular venous pressures, pulmonary congestion, peripheral oedema and body weight; all of which were observed within days of initiation of therapy. In intermediate-term studies, diuretics have been shown to improve cardiac function, symptoms and exercise tolerance in patients with HF. There have been no long-term studies of diuretic therapy in HF and thus, their effects on morbidity and mortality are not known.[2] **Preterm infants with or developing chronic lung disease (CLD):** In preterm infants < 3 weeks of age developing CLD, furosemide administration has either inconsistent effects or no detectable effect. In infants > 3 weeks of age with CLD, a single intravenous dose of 1 mg/kg of furosemide improves lung compliance and airway resistance for one hour. Chronic administration of furosemide improves both oxygenation and lung compliance. Routine or sustained use of systemic loop diuretics in infants with (or developing) CLD cannot be recommended based on current evidence.[3] (LOE II, GOR C) **Aerosolised diuretics for preterm infants with (or developing) chronic lung disease:** In preterm infants > 3 weeks with CLD, administration of a single dose of aerosolised furosemide improves pulmonary mechanics. In view of the lack of data from randomised trials concerning effects on important clinical outcomes, routine or sustained use of aerosolised loop diuretics in infants with (or developing) CLD cannot be recommended based on current evidence.[4] (LOE I GOR C) **Term infants with transient tachypnoea:** Diuretics had no effect in the treatment of transient tachypnoea of the newborn.[5] (LOE I, GOR B) **Preterm infants with respiratory distress (RDS):** There are no data to support routine administration of furosemide in preterm infants with RDS and it may increase the risk of developing a symptomatic patent ductus arteriosus.[6] (LOE I GOR B) **Electively transfused preterm infants beyond the first week of life:** Furosemide resulted in a reduction in post transfusion FiO_2 (0.29 versus 0.27) which may be clinically insignificant.[7] (LOE II, GOR C) **Furosemide for symptomatic patent ductus arteriosus in indomethacin-treated infants:** Use of furosemide in combination with indomethacin increased the incidence of acute renal failure and did not affect the PDA closure rate.[8,9] (LOE II, GOR C) **Infants with post-haemorrhagic ventricular dilatation:** Diuretic therapy is neither effective nor safe in treating post-haemorrhagic ventricular dilatation.[10] (LOE I, GOR B) **Continuous infusion versus intermittent administration of furosemide:** The safety and benefits of continuous infusion of furosemide is unclear.[11–13] In adults and children, no significant increase in urine output except for when loading dose administered prior to infusion.[11] (LOE I, GOR C) **Pharmacokinetics:** Plasma $t_{½}$ of furosemide is 7.7–26.8 hours in neonates. It is lower in immature infants (mean $t_{½}$ > 20 hours)[22]. Drug accumulation may occur with 12 hour dosing especially in infants < 33 weeks PMA.[14] (LOE IV, GOR B)

	The bioavailability of oral furosemide markedly reduced in preterm infants – estimated at 20%[15] compared to ~60% in adults.[16] 94% is plasma protein bound.[15] (LOE IV GOR C) Furosemide is primarily cleared via renal secretion (60–70%).[16] Clearance is reduced in renal impairment. **Safety:** Furosemide results in renal excretion of calcium, sodium, chloride and potassium.[17] Prolonged and high dose use of furosemide, especially in the context of other ototoxic treatments (including aminoglycosides), has been associated with ototoxicity.[18–20] Blood concentrations exceeding 0.05 mg/mL may be associated with ototoxicity.[14] (LOE III-2 GOR B). Prolonged furosemide treatment and treatment combined with acetazolamide is associated with nephrocalcinosis.[10, 21] (LOE I GOR B) Alternate day furosemide may be associated with a lower risk of electrolyte and mineral abnormalities.[23]
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