

Furosemide

Furosemide - Loop Diuretic - NKCC2 Inhibitor

Diuretics / Diuretics

Evidence status: current

ICU High-Yield Summary

Loop diuretic used for acute decongestion when clinically important congestion/volume overload is present. In acute pulmonary edema, whether diuresis is the immediate priority depends on the hemodynamic phenotype; markedly hypertensive pulmonary edema may require rapid ventilatory and vasodilator therapy in addition to, or before the full effect of, diuresis.

Mechanism of Action

Thick Ascending Limb NKCC2 Blockade

1. Reaches its site of action by active tubular secretion (via organic anion transporters) in the proximal tubule, since furosemide is highly protein-bound and not effectively filtered at the glomerulus - this secretion step is impaired in renal impairment, contributing to diuretic resistance independent of dose. 2. Once in the tubular lumen, blocks the Na⁺/K⁺/2Cl⁻ (NKCC2) cotransporter on the luminal membrane of the thick ascending limb of the loop of Henle. 3. This abolishes the lumen-positive transepithelial voltage that normally drives paracellular reabsorption of Ca²⁺ and Mg²⁺, and disrupts the medullary concentration gradient - producing potent natriuresis, diuresis, and loss of Ca²⁺, Mg²⁺, and K⁺. 4. The thick ascending limb normally reabsorbs roughly one-quarter of filtered sodium. Blocking NKCC2 therefore produces substantial natriuresis, while distal-nephron sodium reabsorption and chronic nephron adaptation can limit the net response during continued therapy.

ICU Clinical Reasoning

Why I Choose It

Core IV decongestive therapy for acute heart failure with clinically important congestion or volume overload. | IV administration bypasses the unpredictable, often reduced GI absorption seen in decompensated heart failure with bowel wall edema. | IV administration provides a rapid diuretic onset; in acute pulmonary edema, combine it with phenotype-specific support such as NIV and vasodilators when indicated rather than relying on diuresis alone.

Why I Avoid / Key Limitations

Must reach its site of action via active tubular secretion - a step impaired both by reduced renal function and by competing retained organic anions - contributing to true diuretic resistance independent of the dose given. | Causes significant electrolyte losses (K⁺, Mg²⁺, Ca²⁺) and metabolic alkalosis with repeated dosing. | Can cause ototoxicity with rapid high-dose IV administration, particularly in renal impairment or with concurrent aminoglycosides.

Bedside Pearl

Reassess before you re-dose. Check a spot urine sodium roughly 2 hours after a dose to judge whether the response was adequate, rather than reflexively escalating the dose on a fixed schedule - and remember that a home oral dose is NOT a 1:1 conversion to IV, since oral bioavailability is often meaningfully lower, especially in decompensated heart failure.

Dosing & Administration

Routine ICU Dosing

In acute heart failure with congestion, common contemporary algorithms start loop-diuretic-naïve patients with about 20-40 mg IV furosemide and patients already taking a loop diuretic with an IV dose around 2-2.5 times the home oral furosemide-equivalent dose, then reassess early. A spot urine sodium at about 2 hours (with urine output) can help judge response; institutional protocols and kidney function should guide escalation.

Hemodialysis

Diuretic therapy is generally not relevant once a patient is anuric and fully dialysis-dependent, though furosemide may still be used in select dialysis patients to preserve residual native urine output per nephrology guidance - individualize.

CRRT

Not typically indicated as a primary decongestive strategy once CRRT is providing ultrafiltration, though it may be continued in some cases to preserve residual native urine output - individualize with the care team rather than applying a fixed regimen.

Renal Dose Table

CrCl $\geq$ 30 mL/min: Standard dosing as above; effect may still be somewhat blunted in acutely decompensated states independent of CrCl. | CrCl < 30 mL/min / advanced CKD: Higher doses are often required to achieve an adequate intratubular concentration given reduced tubular secretion - dose escalation, not necessarily more frequent dosing, is the usual strategy; individualize with nephrology input for advanced CKD.

Syndrome-Specific Regimens

Acute Decompensated Heart Failure / Pulmonary Edema - Loop-Diuretic-Naïve: Common contemporary approach: 20-40 mg IV furosemide initially, with early reassessment of urine output and spot urine sodium; escalate if the natriuretic/diuretic response is inadequate. | Acute Decompensated Heart Failure - Chronic Loop-Diuretic User: A common initial strategy is an IV furosemide-equivalent dose around 2-2.5 times the patient's total daily home oral loop-diuretic dose, then titrate to early natriuretic/urine-output response. - The DOSE trial found no significant difference between bolus and continuous-infusion strategies, or between higher- and lower-intensity dosing, on its co-primary endpoints - do not assume continuous infusion is inherently superior to intermittent bolus dosing.

Organ Failure Considerations

Renal Failure & AKI

Higher doses are typically required as renal function declines, since furosemide must be actively secreted into the tubular lumen - a step impaired by reduced GFR and by competition from retained organic anions - to reach its site of action. This is a distinct, pharmacokinetic mechanism of diuretic resistance from the distal-nephron-adaptation mechanism seen with chronic use.

Hepatic Impairment

Use with caution in decompensated cirrhosis with ascites - aggressive diuresis can precipitate hepatorenal physiology, hyponatremia, and hepatic encephalopathy. A more gradual approach, often combined with an aldosterone antagonist, is generally preferred in that specific context rather than the acute-ADHF dosing approach described here.

Toxicity & Safety

Major Warnings

Electrolyte depletion - hypokalemia, hypomagnesemia, and hypochloremic metabolic alkalosis with repeated or high-dose use. | Ototoxicity - tinnitus and hearing loss, usually reversible, with risk increased by rapid high-dose IV administration, renal impairment, and concurrent ototoxic drugs (e.g., aminoglycosides). | Hypotension and pre-renal azotemia with over-diuresis. | Sulfonamide-related hypersensitivity potential (furosemide is a sulfonamide derivative), though true cross-reactivity with antimicrobial sulfonamides is now considered lower-risk than classically taught.

Organ Toxicities

Renal/Electrolyte: Hypokalemia, hypomagnesemia, hypocalcemia (from impaired paracellular Ca^{2+} reabsorption), hypochloremic metabolic alkalosis, and pre-renal azotemia with over-diuresis. | Otolgic: Tinnitus and hearing loss, usually reversible, with rapid high-dose IV administration. | Cardiovascular: Hypotension with aggressive diuresis, particularly in relatively volume-depleted or preload-dependent patients.

Drug Interactions

Bedside Interactions

Aminoglycosides: Additive ototoxicity; consequence: Increased risk of hearing loss; ICU action: Use the lowest effective doses of both agents when concurrent use is necessary, and monitor for auditory symptoms. | Digoxin: Furosemide-induced hypokalemia increases myocardial sensitivity to digoxin; consequence: Increased risk of digoxin toxicity/arrhythmia; ICU action: Monitor potassium closely and replete proactively in patients on concurrent digoxin. | NSAIDs: Inhibit renal prostaglandin synthesis, blunting furosemide's natriuretic effect and renal blood flow; consequence: Reduced diuretic efficacy and increased AKI risk; ICU action: Avoid NSAIDs where possible in patients dependent on loop diuretic therapy for decongestion.

Monitoring & TDM

Monitoring

Urine output and net fluid balance | Serum electrolytes (K^+ , Mg^{2+} , Na^+ , Cl^-) and renal function, at least daily during active diuresis | Spot urine sodium roughly 2 hours post-dose to assess adequacy of natriuretic response | Blood pressure and orthostatic symptoms | Auditory symptoms with high-dose or rapid IV administration

Evidence & Source Traceability

Claim-Level Citations

Contemporary ESC/HFA expert guidance supports early response-guided IV loop-diuretic titration in acute heart failure, commonly using spot urine sodium at approximately 2 hours together with urine output; urine sodium below about 70 mmol/L suggests an inadequate response and should prompt escalation when clinically appropriate. - Heart Failure Association/ESC expert consensus on urinary sodium-guided diuretic titration. Eur J Heart Fail. 2025. (<https://academic.oup.com/eurjhf/article/27/6/940/8468409>) | Current U.S. furosemide labeling indicates IV furosemide for edema and as adjunctive therapy in acute pulmonary edema; rapid/high-dose administration increases ototoxicity risk, especially with severe renal impairment or other ototoxic drugs. - Furosemide Injection U.S. Prescribing Information, DailyMed 2025-2026. (<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d76bd85a-8e57-477e-9607-c9435f1e26fb>) | The DOSE trial found no significant difference in the co-primary endpoints between bolus and continuous infusion, or between higher- and lower-intensity furosemide dosing strategies, in acute decompensated heart failure. - Felker GM, et al. Diuretic Strategies in Patients with Acute Decompensated Heart Failure. N Engl J Med. 2011;364(9):797-805. (<https://pubmed.ncbi.nlm.nih.gov/21366472/>)