Furosemide

Introduction: Furosemide is a diuretic which is an anthranilic acid derivative.

Mechanism of action: Furosemide acts by inhibiting the Na-K-2Cl symporter in the thick ascending limb of the loop of Henle. The action on the distal tubules is independent of any inhibitory effect on carbonic anhydrase or aldosterone; it also abolishes the corticomedullary osmotic gradient and blocks negative as well as positive free water clearance. Additionally, furosemide is a noncompetitive subtype-specific blocker of GABA-A receptors.

Pharmacology:

Bioavailability	Peak plasma level	Plasma half-life	Active metabolites	Elimination
variable*	50% (30-80%)	1 hour	1 to 2 hours	none	predominantly renal

**The variability of the bioavailability is based on the discrepancies of the gastrointestinal absorption (no presystemic metabolism). The urine concentration is more important for the efficacy than the plasma level.*

Indications:

Edema: Furosemide is indicated in adults and pediatric patients for the treatment of edema associated with congestive heart failure, cirrhosis of the liver, and renal disease, including the nephrotic syndrome. Furosemide is particularly useful when an agent with greater diuretic potential is desired.

Hypertension: Oral furosemide may be used in adults for the treatment of hypertension alone or in combination with other antihypertensive agents. Hypertensive patients who cannot be adequately controlled with thiazides will probably also not be adequately controlled with furosemide alone.

Dosage:

Edema: Therapy should be individualized according to patient response to gain maximal therapeutic response and to determine the minimal dose needed to maintain that response.

Adults: The usual initial dose of furosemide is 20 to 80 mg given as a single dose. Ordinarily a prompt diuresis ensues. If needed, the same dose can be administered 6 to 8 hours later or the dose may be increased. The dose may be raised by 20 or 40 mg and given not sooner than 6 to 8 hours after the previous dose until the desired diuretic effect has been obtained. The individually determined single dose should then be given once or twice daily (eg, at 8 am and 2 pm). The dose of furosemide may be carefully titrated up to 600 mg/day in patients with clinically severe edematous states.

Geriatric patients: In general, dose selection for the elderly patient should be cautious, usually starting at the low end of the dosing range.

Pediatric patients: The usual initial dose of oral furosemide in pediatric patients is 2 mg/kg body weight, given as a single dose. If the diuretic response is not satisfactory after the initial dose, dosage may be increased by 1 or 2 mg/kg no sooner than 6 to 8 hours after the previous dose. Doses greater than 6 mg/kg body weight are not recommended. For maintenance therapy in pediatric patients, the dose should be adjusted to the minimum effective level.
Hypertension: Therapy should be individualized according to the patient's response to gain maximal therapeutic response and to determine the minimal dose needed to maintain the therapeutic response.
Adults: The usual initial dose of furosemide for hypertension is 80 mg, usually divided into 40 mg twice a day. Dosage should then be adjusted according to response. If response is not satisfactory, add other antihypertensive agents. Changes in blood pressure must be carefully monitored when furosemide is used with other antihypertensive drugs, especially during initial therapy.
Geriatric patients:In general, dose selection and dose adjustment for the elderly patient should be cautious, usually starting at the low end of the dosing range.

Side effects: Adverse reactions are categorized below by organ system and listed by decreasing severity.
Gastrointestinal System Reactions:

- hepatic encephalopathy in patients with hepatocellular insufficiency
- pancreatitis
- jaundice (intrahepatic cholestatic jaundice)
- anorexia
- oral and gastric irritation
- cramping
- diarrhea
- constipation
- nausea
- vomiting

Systemic Hypersensitivity Reactions:

- systemic vasculitis
- interstitial nephritis
- necrotizing angiitis

Central Nervous System Reactions:

- tinnitus and hearing loss
- paresthesias
- vertigo
- dizziness
- headache
- blurred vision
- *xanthopsia*

Hematologic Reactions:

- aplastic anemia (rare)
- thrombocytopenia

- agranulocytosis (rare)
- hemolytic anemia
- leucopenia
- anemia

Dermatologic-Hypersensitivity Reactions:

- exfoliative dermatitis
- bullous pemphigoid
- erythema multiforme
- purpura
- photosensitivity
- urticaria
- rash
- pruritus

Cardiovascular Reaction: Orthostatic hypotension may occur and be aggravated by alcohol, barbiturates or narcotics.

Precautions:

General: 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. Hypokalemia may develop with furosemide, especially with brisk diuresis, inadequate oral electrolyte intake, when cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially myocardial effects. All patients receiving furosemide therapy should be observed for these signs or symptoms of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, hypokalemia, hypomagnesemia or hypocalcemia): dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, arrhythmia, or gastrointestinal disturbances such as nausea and vomiting. Increases in blood glucose and alterations in glucose tolerance tests (with abnormalities of the fasting and 2-hour postprandial sugar) have been observed, and rarely, precipitation of diabetes mellitus has been reported.

Pregnancy: Category C: 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.

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

Geriatric Use: This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and it may be useful to monitor renal function.

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

How supplied: Customized as per request.