Diuretic Drugs - Site of Action, PK, Uses, Adverse Effects and Notes

Diuretic Class / Drugs	Site of Action & Mechanism	Clinical Uses	Adverse Effects (AEs)	Contraindications & Notes
Carbonic Anhydrase Inhibitors (CAIs) **Drugs: Acetazolamide, Dichlorphenamide, Methazolamide**	Proximal convoluted tubule. Inhibits carbonic anhydrase, reducing NaHCO3 reabsorption by about 85%. Lowers aqueous humor and CSF formation; causes alkaline diuresis.	Glaucoma (most common, topical), urinary alkalinization, metabolic alkalosis, acute mountain sickness, epilepsy adjunct.	Hyperchloremic metabolic acidosis, calcium phosphate renal stones, renal K+ loss, hypersensitivity.	Contraindicated in liver cirrhosis because alkaline urine reduces NH4+ excretion, risking hyperammonemia and hepatic encephalopathy.
Loop Diuretics (high ceiling) **Drugs: Furosemide, Bumetanide, Torsemide (sulfonamides), Ethacrynic acid**	Thick ascending limb of Henle. Inhibits luminal Na+/K+/2Cl- co-transporter (NKCC2). Rapidly absorbed, highly protein-bound, secreted by tubules and filtered. Torsemide has an active metabolite.	Acute pulmonary edema, CHF, acute hypercalcemia, hyperkalemia, acute renal failure, forced diuresis.	Hypokalemic metabolic alkalosis, ototoxicity/deafness (reversible), hypomagnesemia, hyperuricemia, hyponatremia.	Most efficacious diuretics; tolerance does not develop. Induce renal prostaglandin (PGE2) synthesis; antagonized by NSAIDs.
Thiazide Diuretics **Drugs: Hydrochlorothiazide, Chlorthiazide, Chlorthalidone, Indapamide, Metolazone**	Distal convoluted tubule. Blocks electrically neutral Na+/Cl- co-transporter (NCC). Enhances Ca2+ reabsorption. Orally used except chlorthiazide IV. Indapamide is excreted via bile; competes with uric acid for secretion.	Hypertension, edema (mild to moderate CHF, hepatic or renal insufficiency), nephrolithiasis due to hypercalciuria, nephrogenic diabetes insipidus.	Hypokalemic metabolic alkalosis, hyperuricemia, hyperglycemia, hyperlipidemia, hyponatremia, photosensitivity.	Significant carbonic anhydrase inhibitory activity. Actions depend partly on prostaglandins.
K+ Sparing: Aldosterone Antagonists **Drugs: Spironolactone, Eplerenone**	Collecting tubules. Competitively block aldosterone receptors, reducing Na+/H2O reabsorption and K+/H+ excretion. Spironolactone undergoes extensive enterohepatic cycling; active metabolite is canrenone.	Mineralocorticoid excess (primary, secondary, ectopic), used with other diuretics to reduce K+ loss.	Hyperkalemia (dangerous with ACEIs, NSAIDs, etc.), metabolic acidosis, gynecomastia/impotence/BPH with spironolactone only.	Reduce dose in hepatic disease. Ketoconazole and itraconazole increase eplerenone levels via CYP3A4 inhibition.
K+ Sparing: Direct ENaC Blockers **Drugs: Amiloride, Triamterene**	Collecting tubule. Directly interferes with Na+ entry through ENaC, sparing K+. Amiloride is excreted unchanged. Triamterene is metabolized in the liver; active metabolite has shorter t1/2.	Used with other diuretics to reduce K+ loss.	Hyperkalemia, metabolic acidosis. Triamterene only: leg cramps, interstitial nephritis, nephrolithiasis (crystals).	Do not block aldosterone receptors. Acute renal failure if triamterene is given with indomethacin.
Osmotic Diuretics **Drugs: Mannitol, Urea, Glycerin, Isosorbide**	Proximal tubule and descending limb. Filtered but not reabsorbed. Attract water and prevent water reabsorption. Mannitol is not absorbed orally, not metabolized, and is excreted by glomerular filtration.	Prevention of acute renal failure from large pigment load; reduce intracranial and intraocular pressure pre-surgery.	Initial hyponatremia and volume expansion (risk of pulmonary edema/CHF), then dehydration and hypernatremia, hyperkalemia from intracellular dehydration.	Oppose ADH action in collecting tubule. Mannitol increases renal blood flow via prostaglandins.
ADH Antagonists **Drugs: Conivaptan (nonpeptide), Lithium, Demeclocycline**	Collecting tubule. Block V2 vasopressin receptors, reducing cAMP and ADH action. Conivaptan is IV and has a t1/2 of about 5-10 hours.	SIADH.	Nephrogenic diabetes insipidus, severe hypernatremia, dry mouth and thirst, hypotension.	Lithium is nonselective and is not used specifically as an ADH antagonist for this purpose.