D.PHARM • FIRST YEAR

Pharmaceutical Chemistry

CHAPTER 8

Diuretics



ENGLISH CHAPTER NOTES

DIPLOMA IN PHARMACY

DIURETICS: OVERVIEW & CLASSIFICATION

DEFINITION

- Diuretics increase renal excretion of water and electrolytes, especially Na^+.
- More Na^+ remaining in the nephron holds water in the tubular fluid → urine volume increases.
- Reduced extracellular-fluid and blood volume can lower blood pressure, oedema and cardiac workload.

1. CARBONIC ANHYDRASE INHIBITORS

Examples: Acetazolamide, Methazolamide, Dichlorphenamide.

Main site: proximal convoluted tubule.

2. THIAZIDE & THIAZIDE-LIKE DIURETICS

Examples: Chlorothiazide, Hydrochlorothiazide, Chlorthalidone, Benzthiazide, Metolazone, Xipamide.

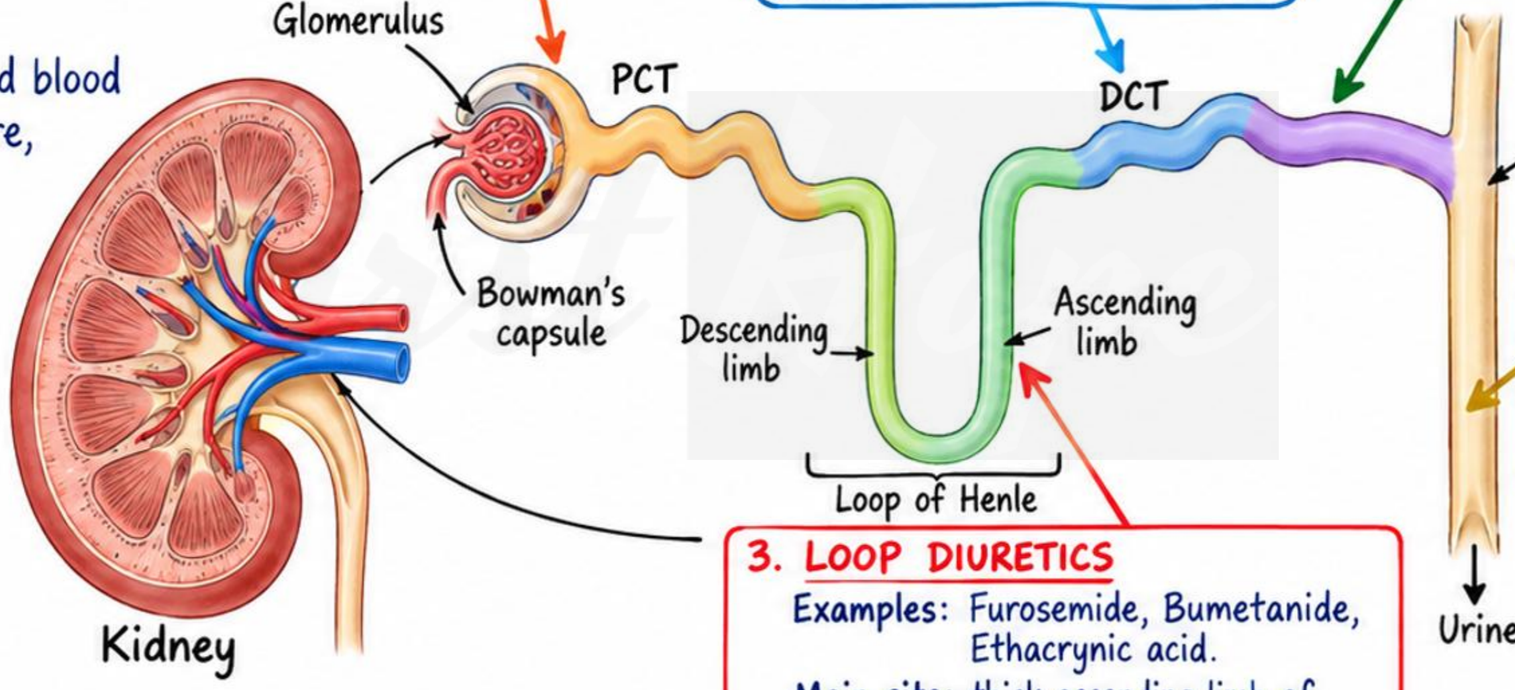
Main site: distal convoluted tubule.

4. POTASSIUM-SPARING DIURETICS

Aldosterone antagonist: Spironolactone.

ENaC blockers: Amiloride, Triamterene.

Main site: late distal tubule and collecting duct.



5. OSMOTIC DIURETICS

Example: Mannitol.

Remain in tubular fluid and hold water osmotically.

3. LOOP DIURETICS

Examples: Furosemide, Bumetanide, Ethacrynic acid.

Main site: thick ascending limb of loop of Henle.

COMMON USES

- Hypertension; heart-failure or other oedema; pulmonary oedema; selected kidney, eye or brain-pressure conditions.

↓ Extracellular-fluid and blood volume → ↓ Blood pressure → ↓ Oedema → ↓ Cardiac workload

NEPHRON SITES & ELECTROLYTE EFFECTS

BASIC SEQUENCE

- Filtered Na^+ enters nephron → transporters reabsorb Na^+ → water follows.
- Diuretic blocks a transporter, enzyme or hormone action → more solute and water remain in tubular fluid → excretion increases.

OSMOTIC EFFECT

- Mannitol increases tubular-fluid osmolality in water-permeable segments → water reabsorption falls.

PROXIMAL CONVOLUTED TUBULE

- Carbonic anhydrase inhibitors block HCO_3^- reabsorption.
- ↑ HCO_3^-, Na^+, K^+ and water excretion; urine becomes alkaline.

THICK ASCENDING LIMB

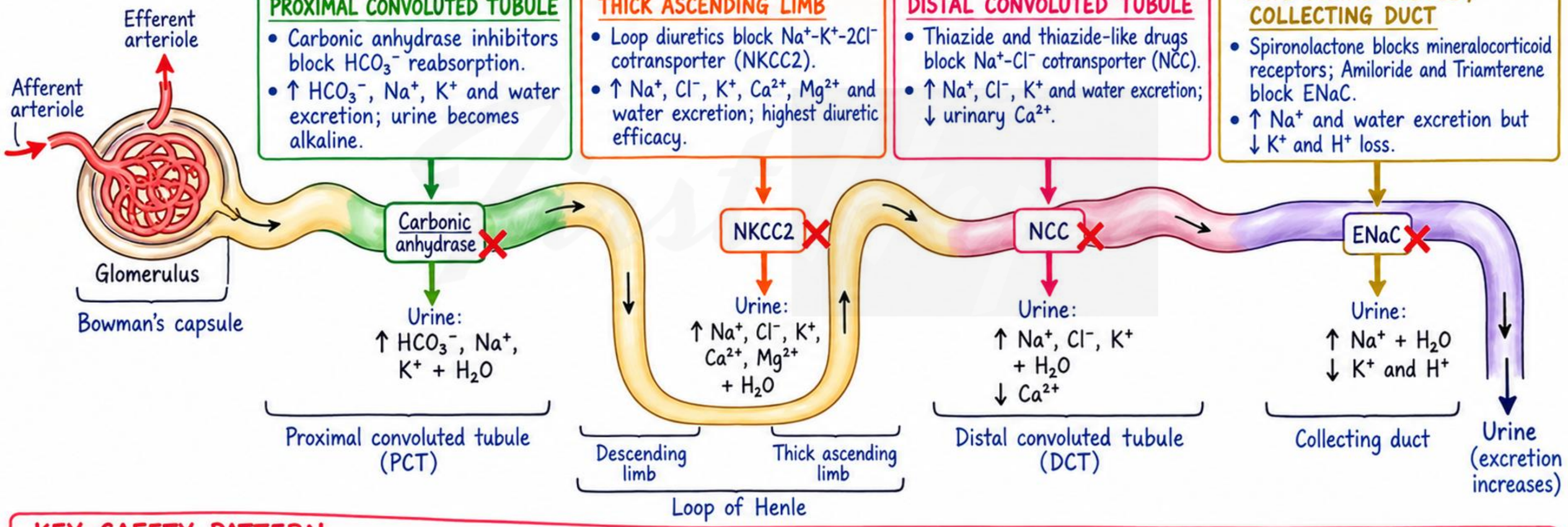
- Loop diuretics block Na^+-K^+-$2Cl^-$ cotransporter (NKCC2).
- ↑ Na^+, Cl^-, K^+, Ca^{2+}, Mg^{2+} and water excretion; highest diuretic efficacy.

DISTAL CONVOLUTED TUBULE

- Thiazide and thiazide-like drugs block Na^+-Cl^- cotransporter (NCC).
- ↑ Na^+, Cl^-, K^+ and water excretion; ↓ urinary Ca^{2+}.

LATE DISTAL TUBULE / COLLECTING DUCT

- Spironolactone blocks mineralocorticoid receptors; Amiloride and Triamterene block ENaC.
- ↑ Na^+ and water excretion but ↓ K^+ and H^+ loss.



KEY SAFETY PATTERN

- Carbonic anhydrase inhibitors → Eletabolic acidosis.
- Loop and thiazide drugs → hypokalaemia and volume depletion.
- Potassium-sparing drugs → hyperkalaemia.
- Mannitol is avoided in anuria and may worsen pulmonary oedema.

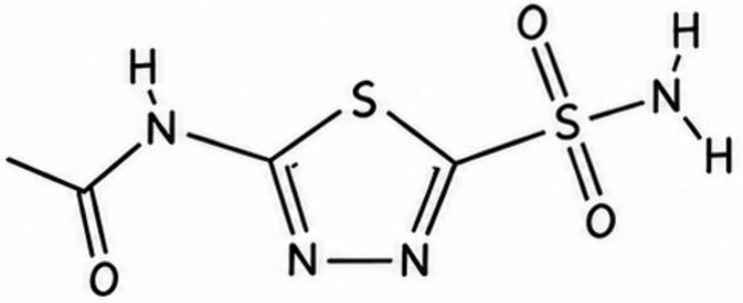
ACETAZOLAMIDE

CLASS

Carbonic anhydrase inhibitor; weak diuretic.

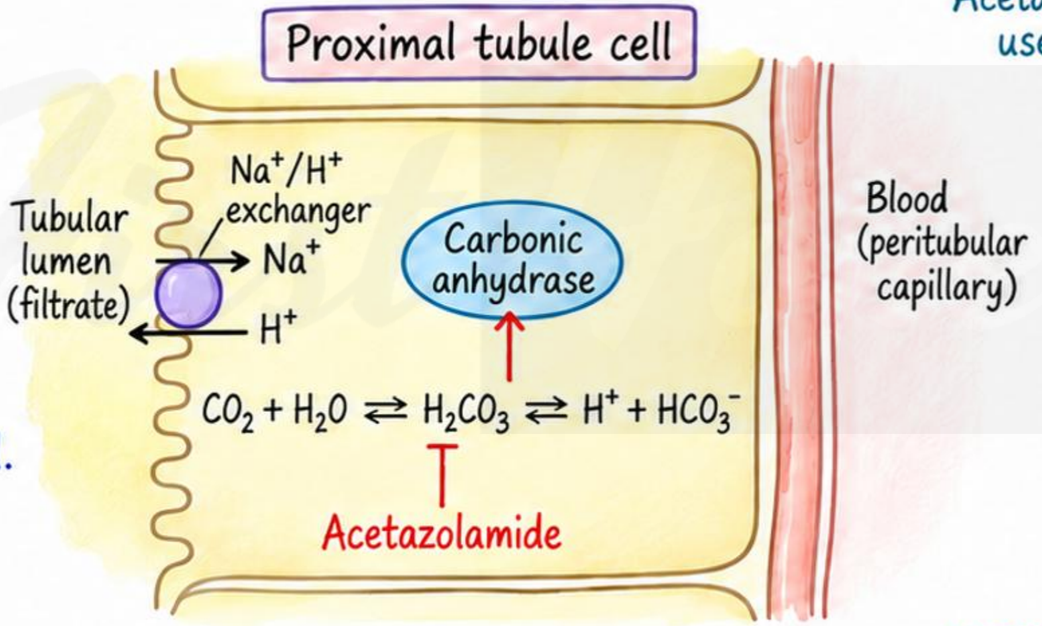
CHEMICAL NAME

N-(5-sulfamoyl-1,3,4-thiadiazol-2-yl)acetamide.

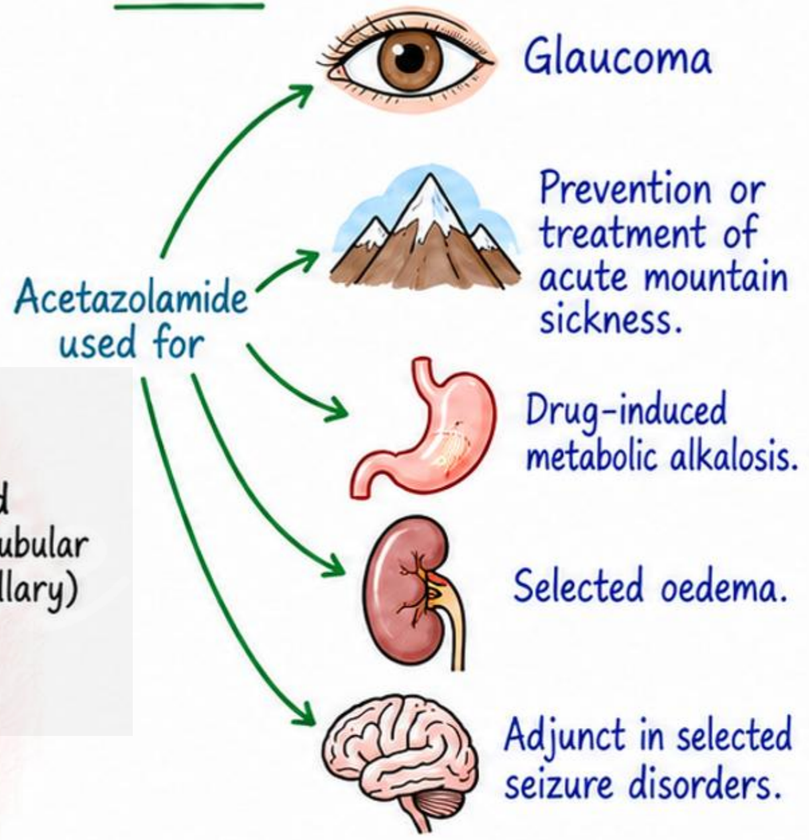


MECHANISM

- Inhibits carbonic anhydrase mainly in the proximal tubule.
- $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$ is slowed.
- Less H^+ is available for Na^+/H^+ exchange and less HCO_3^- is reabsorbed.
- Result: ↑ urinary HCO_3^-, Na^+, K^+ and water; alkaline urine and mild metabolic acidosis.



USES



STABILITY & STORAGE

- Stable when dry. Protect from light and moisture; store at 15–30°C in a well-closed container.

FORMS

- Oral tablets: 125 mg and 250 mg.
- Reconstitutable injection vial: 500 mg.

IMPORTANT EFFECTS

- Paresthesia, fatigue, metabolic acidosis, hypokalaemia and kidney stones may occur.
- Avoid inappropriate use in severe renal or hepatic disease; sulfonamide hypersensitivity is possible.

FUROSEMIDE

CLASS

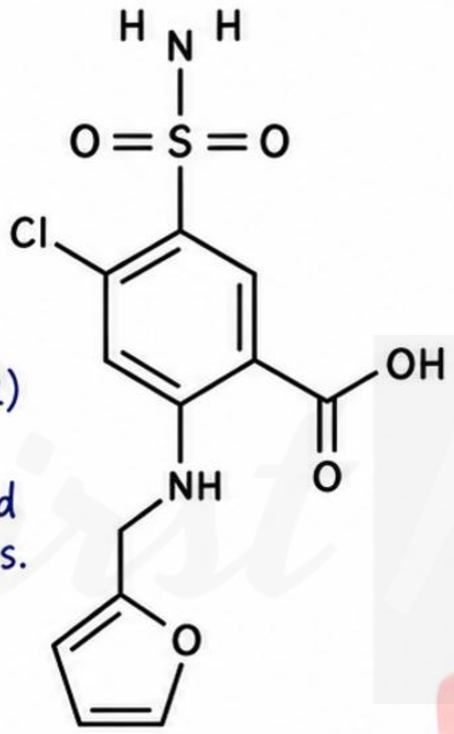
- High-ceiling loop diuretic; also spelled Frusemide in some formularies.

CHEMICAL NAME

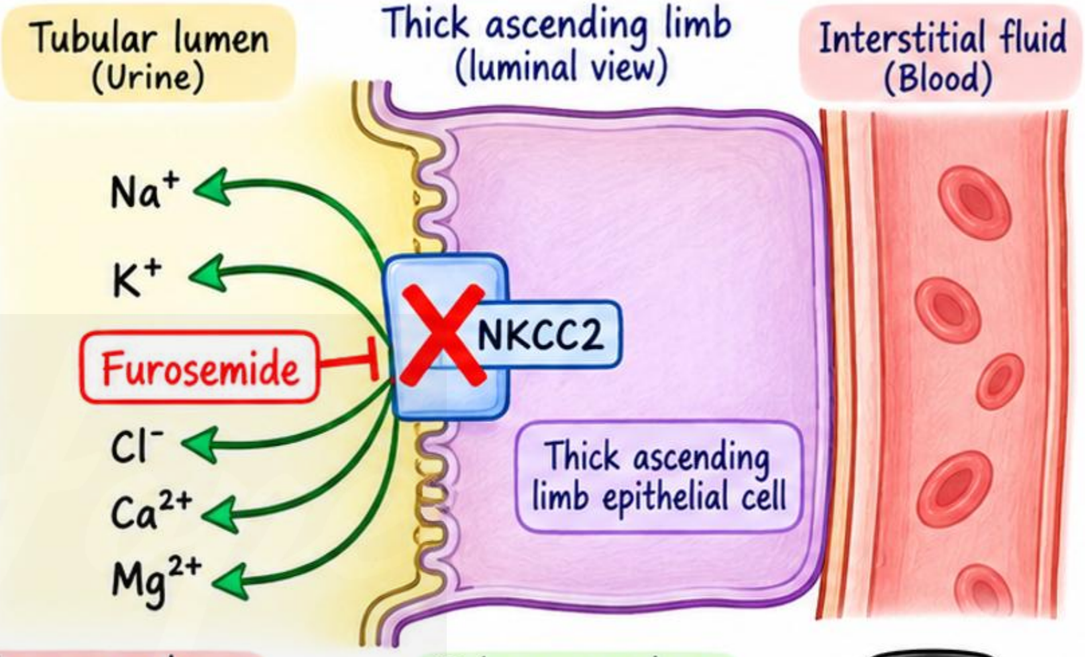
- 4-chloro-2-(furan-2-ylmethylamino)-5-sulfamoylbenzoic acid.

MECHANISM

- Blocks Na^+-K^+-$2Cl^-$ cotransporter (NKCC2) in the thick ascending limb.
- Strongly increases excretion of Na^+, Cl^- and water; K^+, Ca^{2+} and Mg^{2+} loss also increases.
- Reduces venous congestion and pulmonary filling pressure rapidly when given IV.

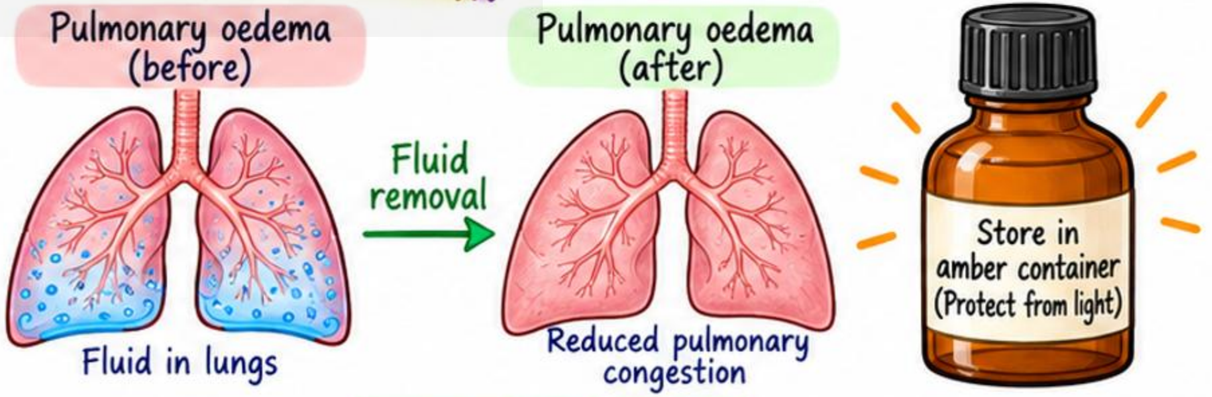


ACTION ON THICK ASCENDING LIMB OF LOOP OF HENLE



USES

- Oedema due to heart failure, hepatic cirrhosis or renal disease.
- Acute pulmonary oedema; hypertension; selected hypercalcaemia.



STABILITY & STORAGE

- Light-sensitive and may photodegrade. Store in an amber, airtight container below 30°C.
- Protect injection from light and freezing; follow the product label after dilution.

FORMS

- Tablets: 20 mg, 40 mg and 80 mg.
- Oral solution: 10 mg/mL. Injection: 10 mg/mL.

IMPORTANT EFFECTS

- Hypokalaemia, hyponatraemia, dehydration, hypotension, hyperuricaemia and metabolic alkalosis may occur.
- Rapid high-dose IV use can cause ototoxicity.

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