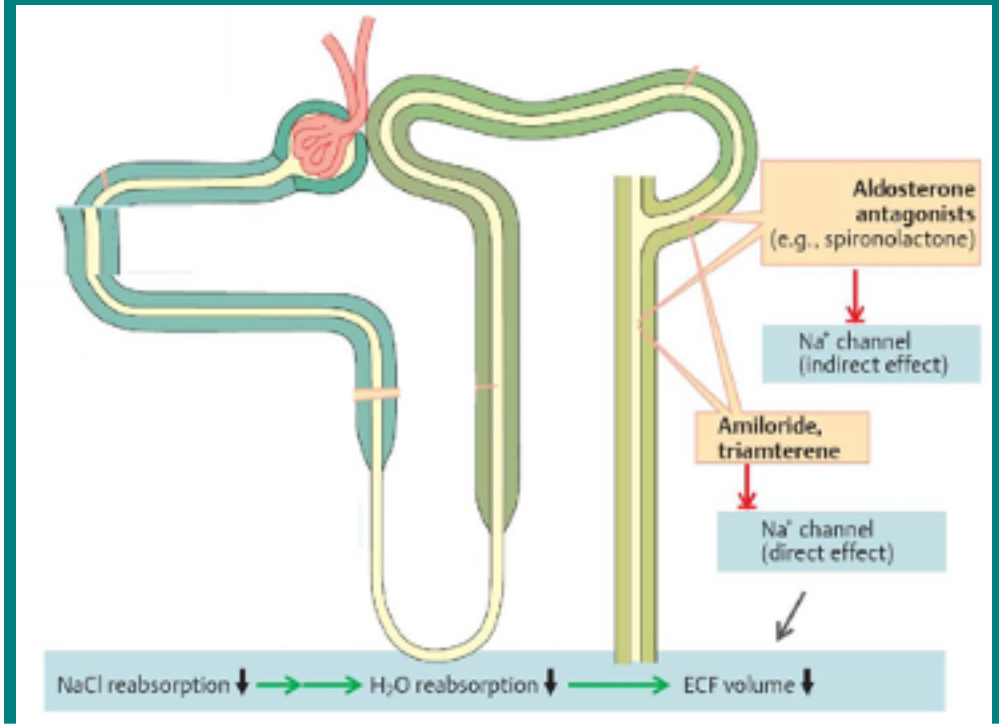
DIURETICS-III

Aldosterone antagonists & Sodium Channel Inhibitors



DIURETICS-III

Potassium-sparing diuretics

Steroidal

Competitive aldosterone antagonists:

- Spironolactone
- Eplerenone

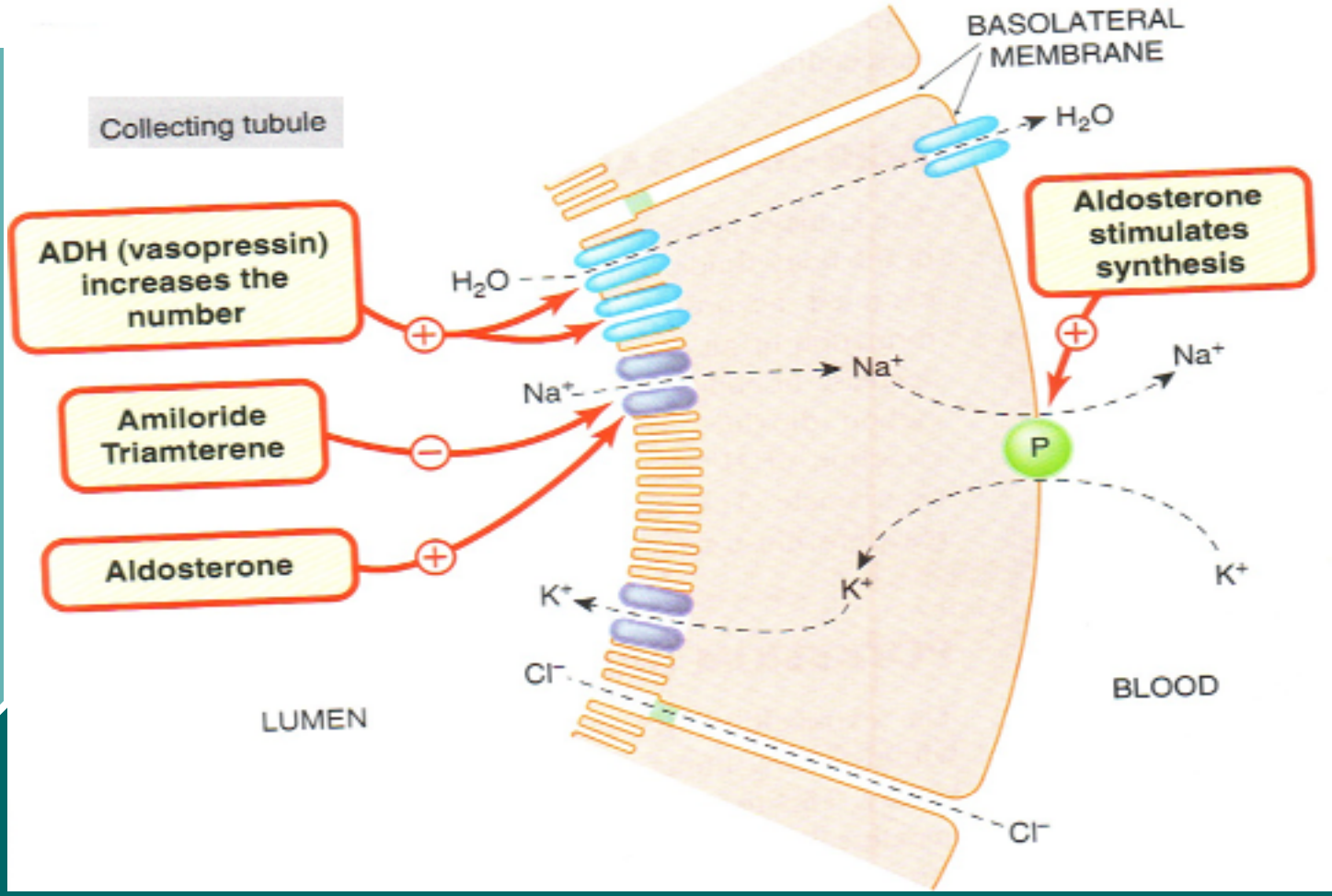
Nonsreroidal

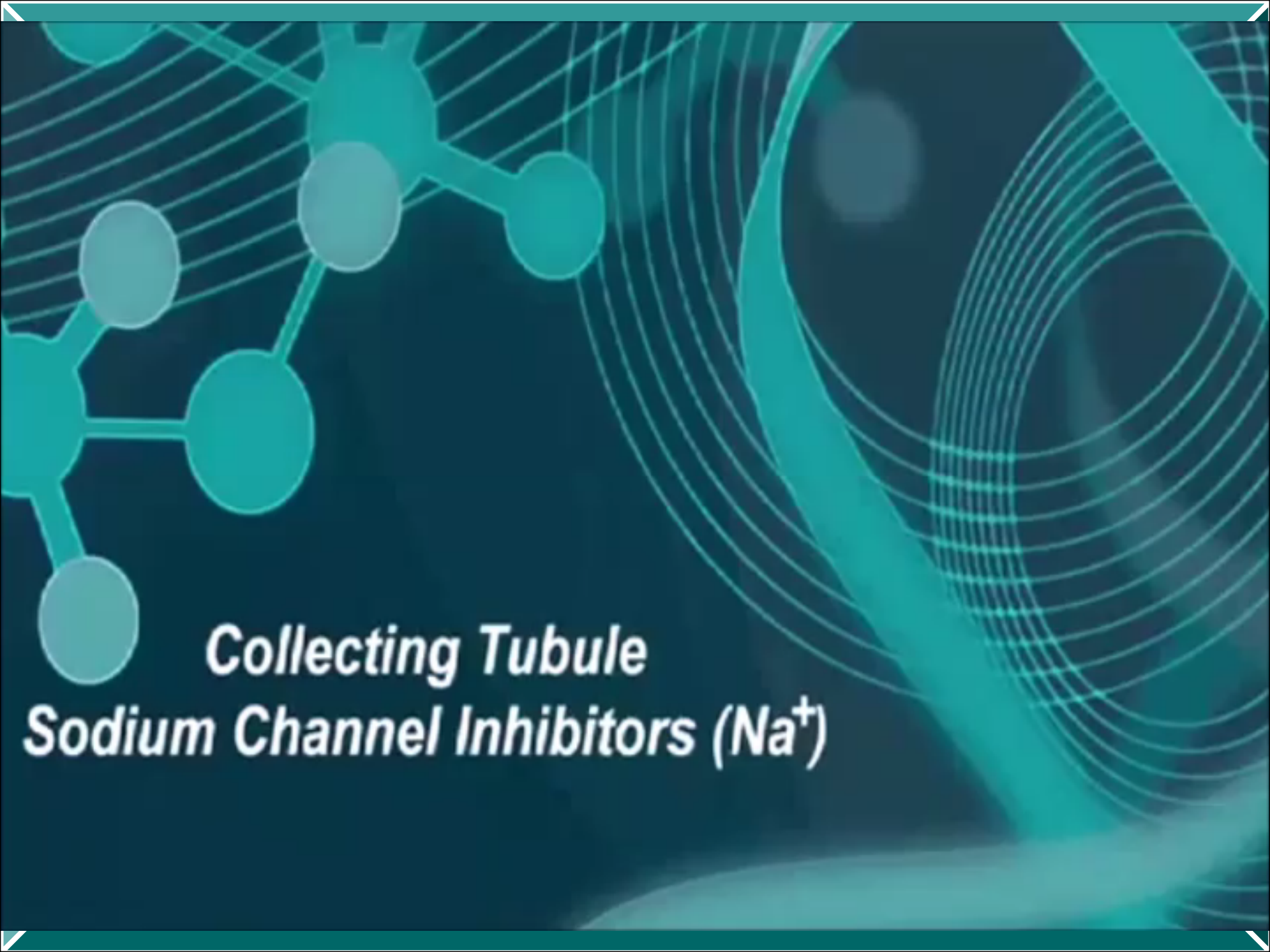
Inhibitors of Na^+ channels:

- Amiloride
- Triamterene

Potassium-sparing diuretics

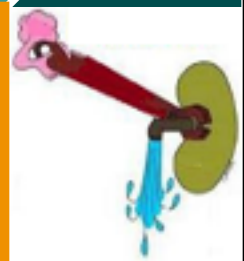
MECHANISM




Collecting Tubule
Sodium Channel Inhibitors (Na^+)

DIURETICS-III

MINERALOCORTICOID RECEPTOR ANTAGONISTS



Also Called:

- K-Sparing Diuretics
- Aldosterone Antagonists

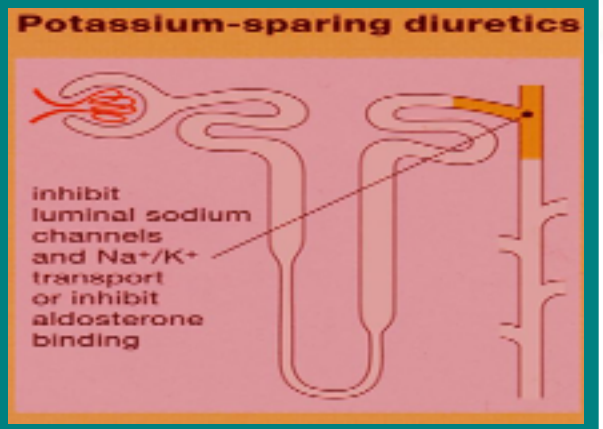
Spironol actone

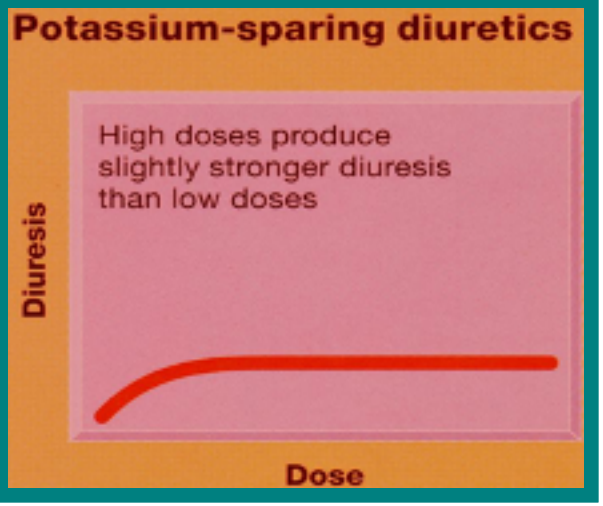
Eplereno ne

ALDOSTERONE ANTAGONISTS

- Aldosterone antagonists are competitive antagonist at the collecting duct→↑ Excretion of Na+,Cl-&↓Excretion of K+,H+,NH4

- Actions depend on renal PGs production





ALDOSTERONE ANTAGONISTS

PHARMACOKINETICS

SPIRONOLACTONE

- Well absorbed from the GIT ,t½=1.6h.

Highly protein- bound

- Undergoes enterohepatic recycling.

- Delayed onset of action (nuclear receptor), maximum diuretic action 4 days.

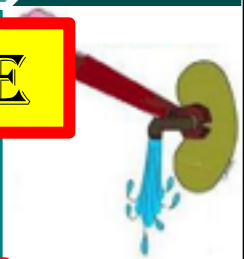
Converted in gut & liver to canrenone [active metabolite, t½=16h].

It binds androgen receptors with high affinity

ALDOSTERONE ANTAGONISTS

PHARMACOKINETICS

EPLERENONE



Eliminated by metabolism(CYP3A4),t½ 5h

Low affinity for progesterone and androgen receptors

Both ineffective in adrenalectomized patients

ALDOSTERONE ANTAGONISTS

THERAPEUTIC USES

Enhances Natriuresis Caused by Other Diuretics

Prevents Hypokalemia

Used in Combination with Loop & Thiazide Diuretics

Blocks Aldosterone

Secondary hyperaldosteronism

Improve survival

Treatment for Heart Failure

Treatment for Primary Hyper-aldosteronism

Treatment for Edema of Liver Cirrhosis

Treatment for Hypertension

Resistant hypertension

Treatment for Nephrotic syndrome

ALDOSTERONE ANTAGONISTS

ADRS

Hyperkalemia

Gastritis

Metabolic Acidosis in cirrhotic patients

Peptic Ulcers

CNS Side Effects

Deepening of Voice

Impotence

Hirsutism

Gynecomastia

Menstrual Irregularities

ALDOSTERONE ANTAGONISTS

DRUG- DRUG INTERACTIONS

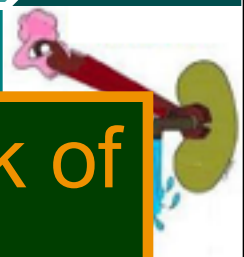
Salicylates → **↓Secretion of canrenone ↓Efficacy of spironolactone**

Digitalis ← **Spironolactone alters clearance**

ALDOSTERONE ANTAGONISTS

CONTRAINDICATIONS

Hyperkalemia



Increased Risk of Hyperkalemia

- Renal failure
- Other K+ sparing diuretics
- ACE-I
- K+ suplement

SODIUM CHANNEL INHIBITORS

Also Called:

- K-Sparing Diuretics

Triamterene
Potency 0.1,
t½ 4.2 h,
elimination
by
metabolism

Amiloride
Potency 1,
t½ 21h,
renal
elimination

SODIUM CHANNEL INHIBITORS

THERAPEUTIC USES

Enhance Natriuresis Caused by Other Diuretics → **Used in Combination with Loop & Thiazide Diuretics**

Prevent Hypokalemia → **Used in Combination with Loop & Thiazide Diuretics**

Block Na+ Channels

- Treatment for Liddle's Syndrome
- Treatment for Lithium-Induced Diabetes Insipidus

SODIUM CHANNEL INHIBITORS

ADRS

Amiloride

Hyperka lemia

Triamterene

Hyperkalemia

Renal Stones

Interstitial Nephritis

Megaloblastosis in cirrhotic patients

SODIUM CHANNEL INHIBITORS

CONTRAINDICATIONS

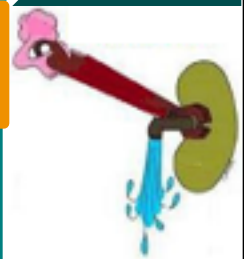
Hyperkalemia

Increased Risk of Hyperkalemia

- Renal failure
- Other K+ sparing diuretics
- ACE-I & ARBs
- Aliskiren
- K+ suplement

SODIUM CHANNEL INHIBITORS

DRUG-Drug INTERACTIONS



ACE Inhibitors
Beta-Blockers
K Supplements
K-Sparing diuretics
Aliskiren

→ **↑Hyperkalemia-induced by K-Sparing diuretics**

DIURETICS

MNEMONIC FOR TYPES

Leak On The CAN

x Na/Cl/K cotransporter

Leak - Loop Diuretics: **Furosemide**

On - Osmotics: **Mannitol, Urea** x Na/Cl cotransporter

The - Thiazides: **Hydrochlorothiazide**

C - Carbonic anhydrase inhibitors: **Acetazolamide**

K sparing

A - Aldosterone inhibitors: **Spironolactone**

N - Na channel blockers: **Amiloride, Triamterene**

Effects	Mechanism of action	Diuretics
↑ Urinary Na HCO3, K Urinary alkalosis Metabolic acidosis	Inhibition of NaHCO3 reabsorption in PCT	CA inhibitors Acetohexamide Dorzolamide
↑Urine excretion ↑ Little Na	Osmotic effect in PCT & DLH	Osmotic diuretic Mannitol
↑Urinary Na, K, Ca, Mg	Na/K/2Cl transporter in TAL the most effective	Loop diuretics Furosemide
↑Urinary Na, K, Mg BUT↓ urinary Ca (hypercalcemia) Metabolic alkalosis	Na and Cl cotransporter in DCT	Thiazide diuretics hydrochlorothiazide
↑ Urinary Na ↓ K, H secretion Metabolic acidosis	competitive antagonist of aldosterone in CCT	K-sparing diuretic Spironolactone.

Uses	Diuretics
Glaucoma, epilepsy Mountain sickness	CA inhibitors Acetohexamide Dorzolamide (topically) for glaucoma
• Cerebral edema • Acute renal failure	Osmotic diuretic Mannitol
Acute pulmonary edema (Drug of choice) Heart failure Hyperkalemia, Hypercalcemia	Loop diuretics Furosemide
Commonly used Hypertension, heart failure, hypercalciuria, kidney stones, diabetes inspidus	Thiazide diuretics hydrochlorothiazide
Hepatic cirrhosis (Drug of choice)	K-sparing diuretic Spironolactone.

Side effects	Diuretics
Metabolic acidosis , Urinary alkalosis Hypokalemia	CA inhibitors Acetohexamide Dorzolamide
Extracellular water expansion Dehydration Hypernatremia	Osmotic diuretic Mannitol
Hypokalemia, hypovolemia, hyponatremia, hypomagnesemia, hypocalcemia Precipitate gout, alkalosis	Loop diuretics Furosemide
Hypokalemia, hyponatremia, hypovolemia, hypomagnesemia, hypercalcemia Alkalosis, precipitate gout Hyperlipidemia, hyperglycemia	Thiazide diuretics hydrochlorothiazide
Gynaecomastia Hyperkalaemia, Metabolic acidosis. GIT upset and peptic ulcer	K-sparing diuretic Spironolactone.

SPIRONOLACTONE