pharmacology of sulphonamides

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JORDAN 2025/2026

Objectives

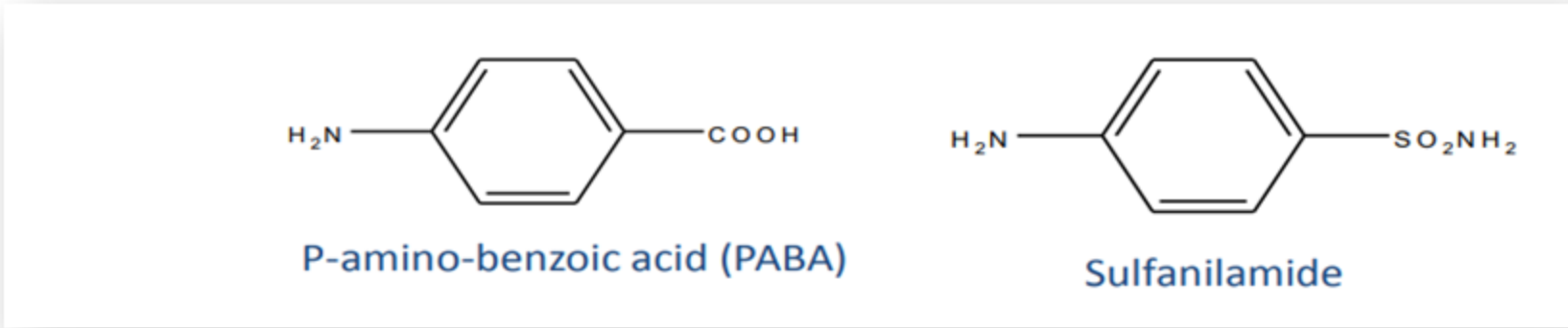
- What are sulfonamides?
- Pharmacodynamics
- Selective toxicity
- Pharmacokinetics
- Co-trimoxazole
- Other sulpha combinations
- Adverse effects
- Contraindications

What are sulfonamides?

- More than 90 years ago (1930s) , sulfonamides changed modern medicine.
- These were some of the first widely used antibiotics, while penicillin soon overshadowed them as an antibiotic
- Sulfonamides are still very commonly used today to different conditions.

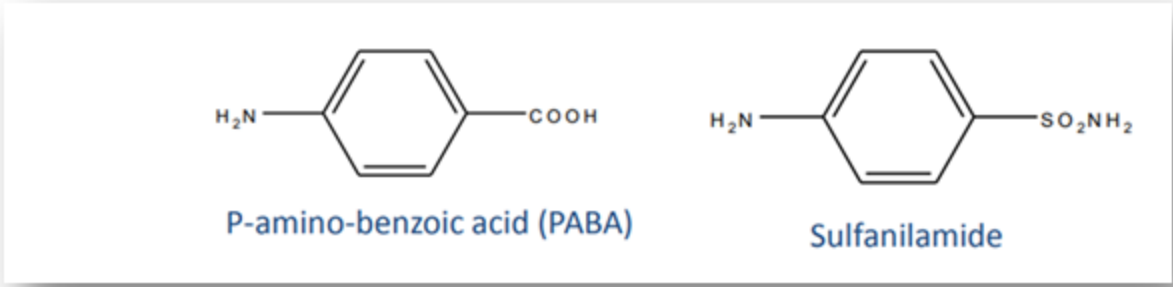
sulfonamides (sulfa drugs)

- **Antimicrobials in this class:**
- **Synthetic**
- **Bacteriostatic**
- **Sulfonamide** is a functional group (a part of a molecule) that is the basis of several groups of drugs, which are called sulphonamides, sulfa drugs or sulpha drugs.



PDs

- Competitive inhibitors of the **enzyme dihydropteroate synthase (DHPS)**, an enzyme involved in folate synthesis.
- Bacterial enzyme DHPS responsible for the incorporation of **PABA** into **dihydrofolic acid** (immediate precursor of folic acid).
- Folic acid required for synthesis of purines and nucleic acid
- Sulfonamides are structural analogue of P-aminobenzoic acid (PABA)



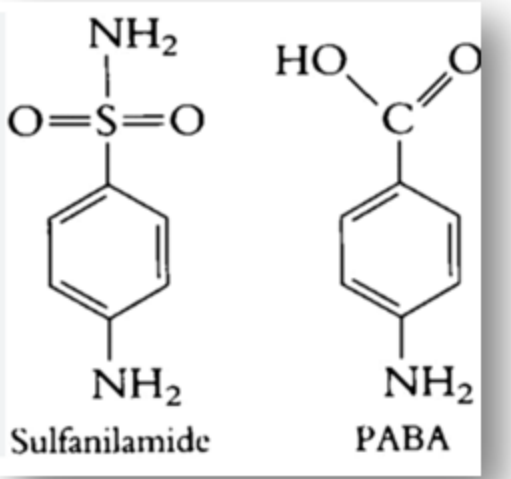
Mechanism of action:

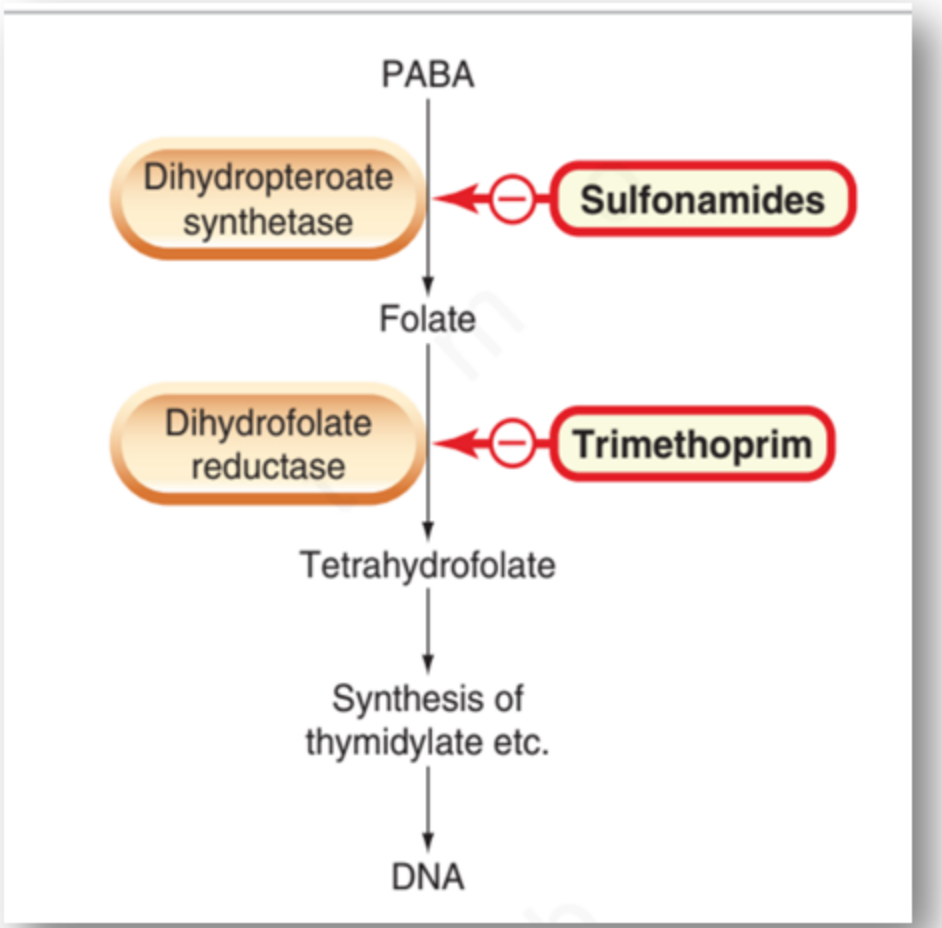
1- Mimic PABA: Sulfonamides are structural analogs of PABA, a natural substrate bacteria use to make folate.

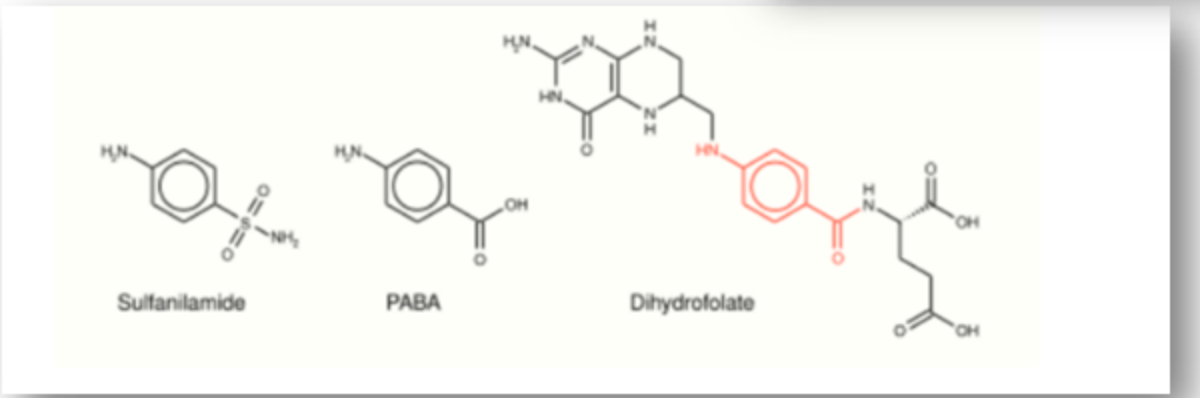
2- Inhibit enzyme: They competitively bind to the active site of dihydropteroate synthetase, preventing it from using PABA.

3- Block folate production: This stops the crucial step in the folate synthesis pathway.

4- Inhibit DNA/RNA synthesis: Without folate, bacteria can't produce purines, essential for DNA and RNA, halting bacterial replication and growth.







Selective toxicity

- Humans, in contrast to bacteria, **acquire folate (vitamin B9) through the diet.**
- This difference: bacteria need to synthetize folate, while humans getting it from diet: humans cannot synthesize folic acid.
- **Creating a specific target**, making sulfa drugs bacteriostatic (growth-inhibiting) against microbes while being safe for hosts, though resistance and allergies limit use.

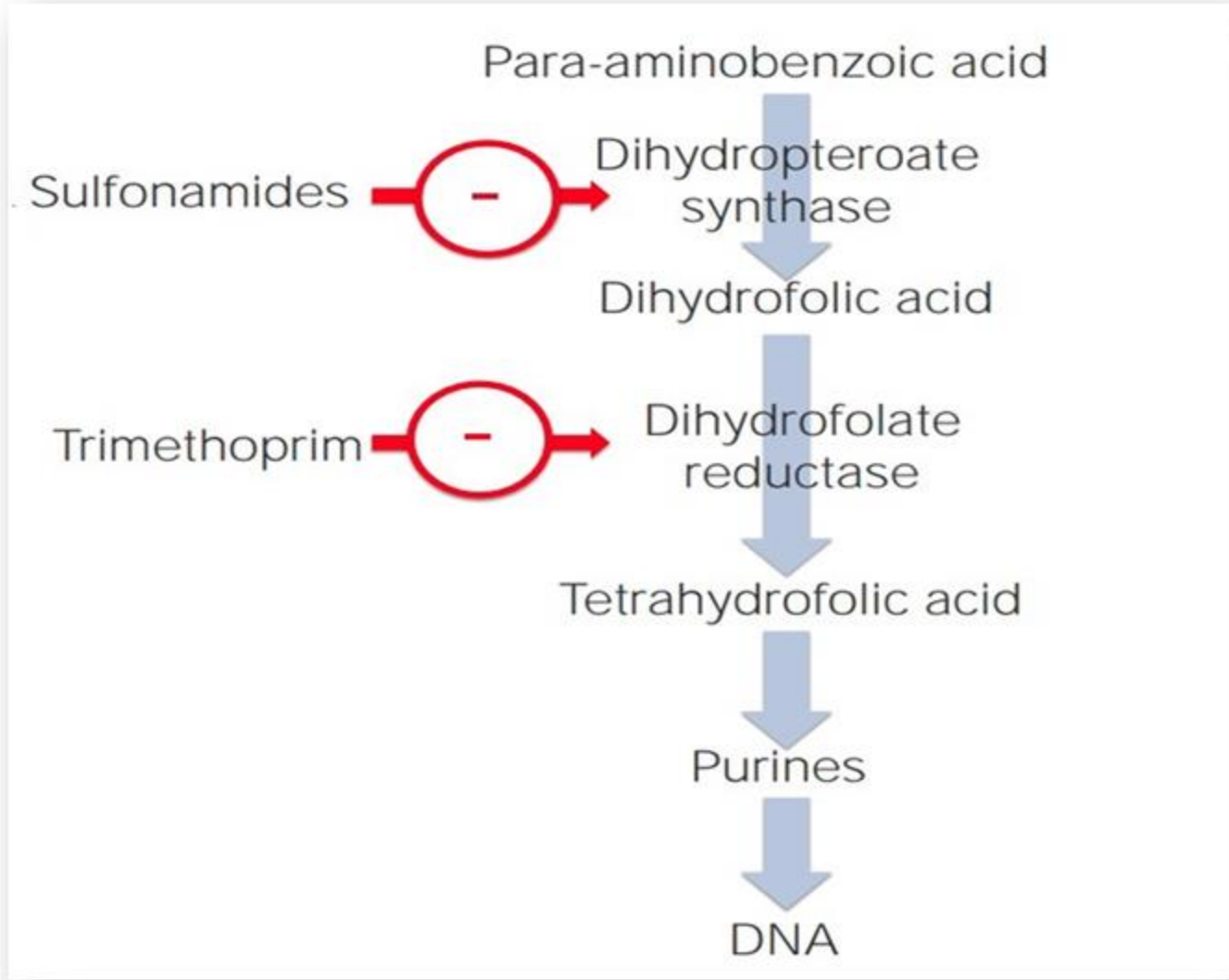
Pharmacokinetics

Absorption	▪ Most of sulfa drugs have **good oral absorption** example: sulfamethoxazole (not affected by food) ▪ **Poor oral absorption**: sulfaguanidine ▪ **Topical**: silver sulfadiazine in burns
Distribution	▪ **BBB**: PASS: used with penicillin for treatment of bacterial meningitis in 1930s-1940s ▪ Good tissue penetration: prostate ▪ **Placenta**: pass ▪ Excreted in breast milk ▪ Sulfonamides **bind significantly to plasma proteins**, primarily **albumin**: (subdomain IB) on albumin, shared with other drugs like warfarin: compete for the same sites, displacing sulfonamides and increasing free drug.
Metabolism	▪ **In the liver**: Acetylation: Forming inactive N4-acetyl metabolites (less soluble). Hydroxylation.
Excretion	**Renal**: acetylated active metabolites (UTIs, alkalization of urine)

Co-trimoxazole

- Sulfamethoxazole with **trimethoprim** in 5: 1
- **Tablets contain** 400 mg of sulfamethoxazole plus 80 mg of trimethoprim.
- **Mechanism of action**:
- Trimethoprim **inhibits the enzyme dihydrofolic acid reductase** (**sequential block)**
- **Bacteriostatic activity**.
- **Spectrum:**
- **Some G+ve**: streptococcal tonsillitis, pharyngitis
- **Some G-ve**: E.coli: UTIs
- **Atypical bacteria**: chlamydia: eye, genital
- **Toxoplasma**
- **Plasmodium falciparum: malaria**
- **Pneumocystis carinii**

Synergism of co-trimoxazole



Indications of co-trimoxazole

- **1- UTIs**: excreted in high concentration in urine (alkalization of urine)
- **2- Streptococcal infections:** pharyngitis, tonsillitis
- **3- Pneumocystis carinii pneumonia (PCP), now called Pneumocystis jirovecii pneumonia (PJP):** serious fungal lung infection hitting people with weakened immune systems, like those with HIV/AIDS, cancer, or organ transplants, causing fever, dry cough, and shortness of breath: co-trimoxazole (Bactrim): oral or IV for 3 weeks
- **4- Toxoplasmosis of CNS**

Other sulphonamides combinations

- **Silver Sulfadiazine (cream)**

•Inhibits growth of nearly all pathogenic **bacteria (pseudomonas)** & **fungi**

•**Used topically** to reduce incidence of infections of wounds from burns

- **Mechanism of action:**

1- Cell Wall/Membrane Damage: **Ionic silver (Ag)** binds to cell structures, disrupting the membrane causing leaks and bacterial death (**bactericidal**).

2- sulfadiazine part: blocking para-aminobenzoic acid (PABA) to prevent folic acid synthesis, which bacteria need for growth.

(Synergistic Effect)

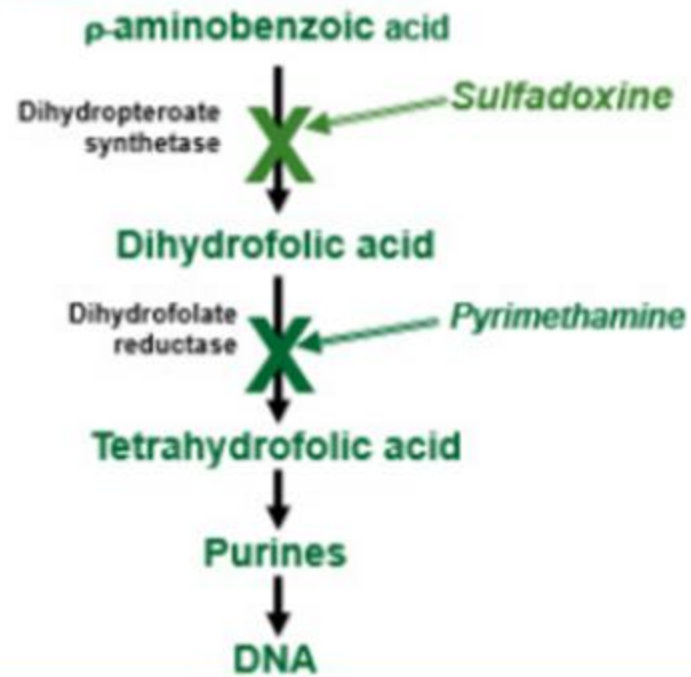
Sulphadoxine and pyrimethamine (fansidar)

- **Sulfadoxine and pyrimethamine (SP) (Fansidar):** combination medication primarily used for **the prevention and treatment of malaria,** particularly in areas with chloroquine-resistant strains.
- **Mechanism of action**:(sequential block)
- Sulfadoxine inhibits the enzyme dihydropteroate synthetase.
- Pyrimethamine inhibits dihydrofolate reductase.

Fansidar mechanism of action

Pyrimethamine and Sulfadoxine (Fansidar)

- Both have long half-lives
- Sequential disruption of essential folate pathway
- Similar toxicity profile



Adverse effects

- 1- **Allergy**:
- Skin rash: common
- Photosensitivity
- Stevens-Johnson syndrome (SJS) (TEN: toxic epidermal necrolysis): rare
- **2- Crystalluria**
- Insoluble in acidic urine
- Precipitate, forming crystalline deposits that can cause urinary obstruction
- Fluid intake sufficient to ensure a daily urine volume of at least 1200ml
- Alkalinization of the urine

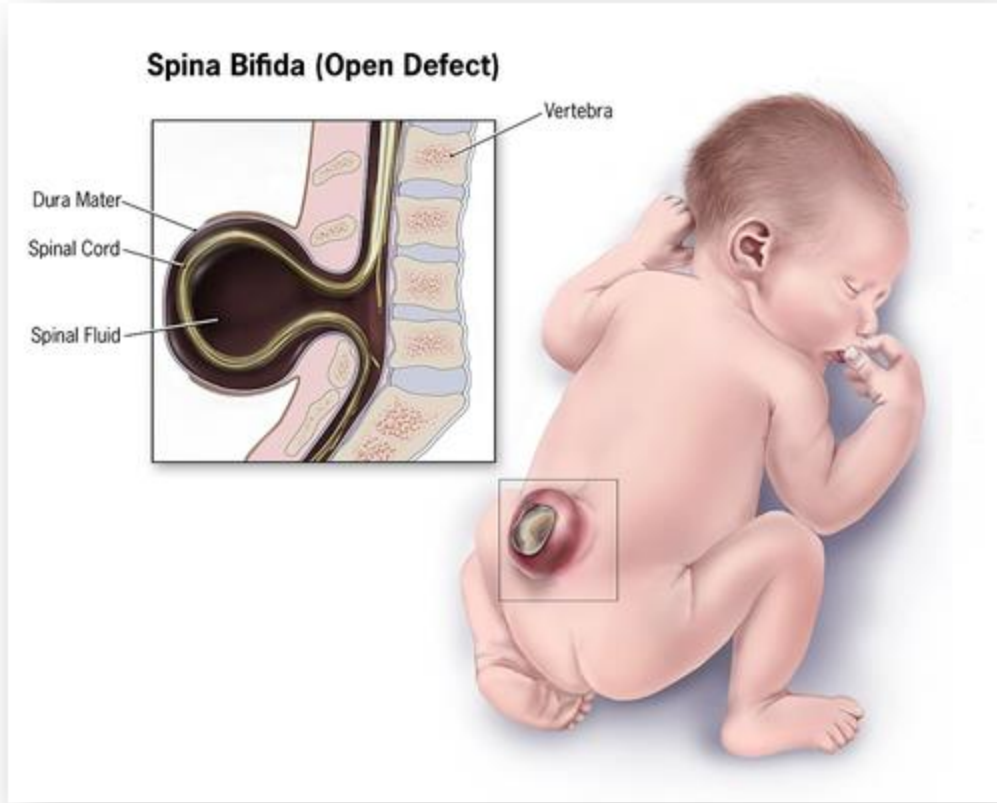
3- kernicterus

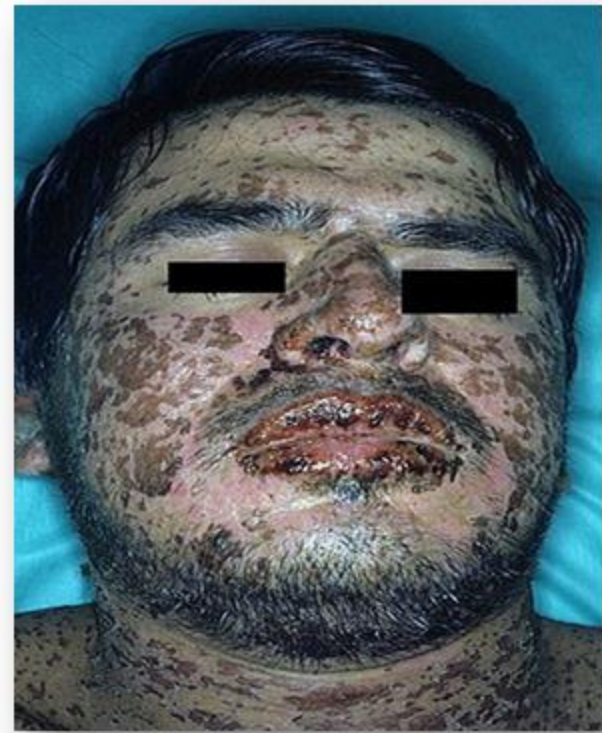
- Administration to **newborn infants esp. premature**
  - Sulfonamides displace **bilirubin (jaundice)** from plasma albumin.
  - Free bilirubin is deposited in **basal ganglia & sub-thalamic nuclei** of the brain causing an encephalopathy & permanent brain damage called **kernicterus**.

- **4- anemia**:
- Hemolytic anemia: G6PD deficiency
- Megaloblastic anemia: treated by folic acid tab. 5 mg once daily:
- Some sulfonamide drugs, such as sulfasalazine, can interfere with intestinal absorption of dietary folate in humans, potentially triggering deficiency, especially in patients with pre-existing conditions like inflammatory bowel disease or poor diet.
- **5- during pregnancy**:
- 1st trimester: neural tube defect (spina bifida): teratogenic
- 3rd trimester: kernicterus

Contraindications

- Pregnancy
- Children less than 2 y
- Allergy to sulpha
- Fauvism
- Renal stones





Stevens-Johnson syndrome (SJS)

References

Lippincott's Illustrated Review

Pharmacology, 8th edition

Lippincott Williams & Wilkins

Katzung *by Anthony Trevor, Bertram Katzung, and Susan Masters . 16th edition McGraw Hill,*

Rang & Dale's Pharmacology: *by Humphrey P. Rang ; James M. Ritter ; Rod Flower Churchill Livingstone; 10th edition*

THANK YOU