

Sulfadiazine

Class:

Sulfadiazine is a sulfonamide

Antiparasitic Activity:

Sulfonamides are synthetic drugs with low potency against a wide range of parasitic organisms including *Plasmodia*, *T. gondii* and *P. carinii*.

Mechanism of Action:

Sulfonamides act through inhibition of dihydropteroate synthetase. Resistance arises through multiple mutations in this gene.

Pharmacokinetics:

Sulfadiazine is rapidly and extensively absorbed from the gut and is 20 to 55% bound to plasma proteins. $T_{1/2}$ is 7-12 hours. Sulfadiazine crosses the placenta achieving blood concentrations in the fetus of 50 to 90% of those in the mother. Sulfadiazine achieves high concentrations in breast milk (20% of plasma).

Dosage:

Toxoplasma gondii:

Several drug combinations are used to treat life-threatening toxoplasma infections in the immune-suppressed; most commonly sulfadiazine is combined with pyrimethamine. A single loading dose of the combination (sulfadiazine 75 mg/kg [maximum daily dose 4g]; pyrimethamine 2 mg/kg [usually 200 mg daily]) is followed by lower daily doses (sulfadiazine 100 mg/kg daily in divided doses; pyrimethamine 1 mg/kg once daily).

Adverse Effects:

The adverse effects of sulfonamides may be considered for the group as a whole. Differences in frequency and severity of reactions are largely a function of elimination rate: bizarre reactions to slowly eliminated drugs being more severe because drug exposure is longer. Most are of a 'type B' or bizarre type and many are thought to involve the immune system. They include fever, arthralgia, bone marrow adverse reactions including neutropaenia, agranulocytosis, and aplastic anaemia, rashes which range from the trivial to the life-threatening and methemoglobinemia and haemolysis in patients with glucose-6-phosphate dehydrogenase deficiency. The commonest serious type A adverse reaction is crystalluria.

Pregnancy:

Sulfadiazine is a sulfonamide antimicrobial that, when administered during the last trimester of pregnancy, theoretically could compete with bilirubin for plasma proteins and exacerbate neonatal jaundice.

Drug Interactions:

Sulfonamides generally are prone to adverse drug interactions by three principal mechanisms:

- Displacement from plasma protein binding
- Inhibition of biotransformation
- Additive pharmacodynamic response

The first two mechanisms, occurring together, explain the 'toxic' potentiation of several drugs with the following common characteristics:

- Cleared by biotransformation to a large degree
- Extensively bound to plasma proteins
- Narrow therapeutic range

Included in this list are: warfarin (and other coumarins), sulfonyleureas and phenytoin

Brand name/Manufacturer:

Microsulfon™. Sulfadiazine (500mg).