DAPSONE

Class:
Dapsone (4, 4’-diaminodiphenylsulfone) is a sulfone

Antiparasitic Activity:
Dapsone is active against *P. falciparum in vitro*, but is invariably combined with a dihydrofolate reductase-inhibitor. (e. g. chlorproguanil or pyrimethamine). Dapsone has activity against *T. gondii* and *P. carinii* in experimental systems.

Mechanism of Action:
Dapsone is an inhibitor of dihydropteroate synthetase (DHPS).

Mechanism of Resistance:
Resistance occurs through multiple mutations in this gene.

Pharmacokinetics:
Absorption is slow but bioavailability is moderately high. The drug is about 70% bound to plasma protein (mainly to albumin). Dapsone is extensively metabolized (by acetylation, hydroxylation and conjugation). The $t_{1/2}$ of dapsone is about 30 hours.

Adverse Effects:
Overdoses of greater than 1.5 g (in adults) can cause life-threatening toxicity including features of haemolysis and methaemoglobinemia, jaundice and coma. Pyrimethamine-dapsone, when used for malaria prophylaxis at a frequency of more than one dose per week, caused agranulocytosis with an estimated prevalence of 1 per 2000-5000 prescriptions. Allergy is well-recognized in patients on long-term therapy and manifests as rash (sometimes life-threatening), fever, hepatic dysfunction, albuminaemia and occasionally organic psychosis. Dapsone is excreted in breast milk in substantial amounts and haemolytic reactions can occur in neonates.

Dosage:
Dapsone is combined with chlorproguanil in LapDap™ which comprises 2.0 and 2.5 mg/kg respectively of chlorproguanil and dapsone. It is given daily for three days for the treatment of uncomplicated falciparum malaria.

Dapsone is also combined with pyrimethamine in a fixed-ratio combination (dapsone 100 mg and pyrimethamine 12.5 mg; Maloprim™) but this is no longer recommended because of adverse effects.

Pregnancy:
Dapsone does not increase the risk of fetal abnormalities if administered during all trimesters of pregnancy or can affect reproduction capacity. Because of the lack of animal studies or controlled human experience, Dapsone should be given to a pregnant woman only if clearly needed

Drug Interactions:
Folic acid antagonists such as pyrimethamine may increase the likelihood of haematological reaction

Brand names/Manufacturer:
Maloprim™ Glaxo SmithKline (pyrimethamine 12.5mg, dapsone 100mg)
Lapdap™; Glaxo SmithKline (chlorproguanil 80 mg + dapsone 100 mg per caplet, for adults, and chlorproguanil 15 mg +dapsone 18.75 mg per caplet for children).