Data Sheet

Dapsone

1. Dapsone 25 mg and 100 mg tablets

Presentation

Tablets: white, scored (100's)

Active: 25mg and 100mg dapsone

2. Uses
3. Actions

Antileprotic/Anti-infective/Anti-fungal.

Dapsone has an action similar to that of sulfonamides, which involves the inhibition of folic acid synthesis in susceptible organisms. It has been suggested that Dapsone may act as an immunomodulator when used to suppress dermatitis herpetiformis.

4. Pharmacokinetics

Absorption: Dapsone is slowly absorbed from the gastrointestinal tract with an absorption half-life of 1.1 hours. Overall bioavailability is 70-80%; may be less in patients with severe leprosy. An acidic environment is needed for optimal absorption.

Distribution: Dapsone is well distributed throughout the total body water and is found in all tissues, especially liver, muscle, kidneys and skin. Saliva concentrations are 18-27% of corresponding plasma Dapsone concentrations. Dapsone also crosses the placenta.

Vol_D - 1.5L per kg (1.9L per kg when given with pyrimethamine)

Protein Binding: Dapsone - moderate to high (70-90%);

Monoacetyl Dapsone (MADDS) - Very high (99%).

Biotransformation: Dapsone is acetylated by N-acetyl transferase in the liver to its major metabolite, monoacetyl Dapsone (MADDS). MADDS is also deacetylated to Dapsone; equilibrium is reached within a few hours. Patients may be divided into slow or fast acetylators. However, unlike with other medications, no relationship has been seen between acetylator type and side effects. There was also no significant difference between the 2 groups in plasma concentrations or pharmacokinetics; therapeutic response was the same in both groups.

Dapsone is also N-hydroxylated to Dapsone hydroxylamine in the liver by the mixed oxidase system in the presence of oxygen and NADPH, and appears to be responsible for the drug's haematologic toxicity.

Both major metabolites have very low activity and do not contribute to the therapeutic effect of Dapsone.

Elimination Half life: 10 to 50 hours (average, 30 hours) for both Dapsone and MADDS. Time to peak serum concentration is 2 to 6 hours, but variable.

Indications

Dermatitis herpetiformis. Leprosy. Actinomycotic mycetoma.

Dosage and Administration

Tablets should be taken whole and small doses should be made up from 25 mg tablets. Do not split the tablet.

Dermatitis herpetiformis.

Adults The usual maintenance dosage is 50 to 100mg daily, but as little as 50mg weekly may be adequate. Dosages of up to 300mg daily may be considered, but efforts should be made to reduce this to the minimal maintenance dosage as soon as possible.

Leprosy.

Adults The standard dose is 100mg daily (1 to 2 mg/kg bodyweight).

Children Dosage should be adjusted according to bodyweight. Those aged 10 to 14 years daily doses of Dapsone 50mg or 1 to 2 mg per kg if their body weight is low, can be given.

The modern treatment of leprosy involves the use of multiple drug regimens to avoid the development of resistant strains. The World Health Organisation has made the following recommendations for standard adult treatment regimens (with dosage adjustments according to bodyweight).

Multibacillary leprosy.

Adults Rifampicin 600mg once monthly supervised; Dapsone 100mg daily, self-administered; Clofazimine 300mg once monthly, supervised; and 50mg daily self-administered.

Children Dosage should be adjusted according to bodyweight for all three drugs, for those aged 10 to 14 years daily doses of Dapsone 50mg or 1 to 2 mg per kg if their body weight is low, can be given.

Paucibacillary leprosy.

Adults Rifampicin 600mg once monthly for 6 months, supervised; Dapsone 100 mg daily for 6 months, self-administered.

Children Dosage should be adjusted according to bodyweight for both drugs, for those aged 10 to 14 years daily doses of Dapsone 50mg or 1 to 2 mg per kg if their body weight is low, can be given.

Actinomycotic mycetoma.

Adults Published reports suggest that a dose of 100mg should be given twice daily and continued for some months after the clinical symptoms have disappeared. Streptomycin at 14mg/kg daily for the first month and alternate days thereafter (or the equivalent) should always be used in combination with Dapsone. Streptomycin sulfamethoxazole trimethoprim is an alternative therapy.

Contraindications

Hypersensitivity to Dapsone and/or it's derivatives.

Dapsone should be administered with caution in patients with renal or hepatic failure and in patients with glucose-6-phophate dehydrogenase deficiency.

Warnings and Precautions

Use with Caution

Dapsone should be used with caution in patients with cardiac, pulmonary, hepatic or renal disease.

Routine haematological analysis should be carried out during long-term therapy with sulfones, because the danger of haemolytic anaemia. The haemolytic effect of sulfones may be exaggerated in glucose-6-phosphate dehydrogenase deficient individuals.

Carcinogenicity

Dapsone in high doses has been reported to be carcinogenic in rats and mice, but negative in Salmonella mutagenicity assays. The relevance of this finding to human exposure is unclear.

5. Use in Pregnancy

(Category B2). The sulfone drugs are generally contraindicated in pregnancy and therefore the use of Dapsone during pregnancy should be avoided unless, in the judgment of the doctor, potential benefit outweighs the risk. Animal reproduction studies have not been conducted with Dapsone. Dapsone is excreted in breast milk in therapeutic amounts. Sulfones may cause haemolytic anaemia in glucose-6-phosphate deficient neonates.

6. Use in Lactation

Should not be used by lactating mothers since Dapsone is excreted in substantial amounts in breast milk.

7. *Effect on the ability to drive or use machinery*

Presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

Adverse Effects

Most adverse reactions are dose related and uncommon at dosages up to 100mg daily. They include anorexia, nausea, vomiting, headache, dizziness, tachycardia, nervousness, insomnia, and skin disorders. Agranulocytosis, peripheral neuritis and psychosis have also been reported. Varying degrees of dose-related haemolysis and methaemoglobinemia occur in most individuals given more than 200mg daily. Dosages up to 100mg daily are unlikely to cause haemolysis, but individuals with glucose-6-hydrogenase deficiency may be affected by dosages above 50mg daily. Rare reactions include the 'Dapsone syndrome' and hypoalbuminemia.

The "Dapsone syndrome" is a hypersensitivity reaction, which develops rarely and tends to occur during the first 6 weeks of therapy. Symptoms may include fever, eosinophilia, mononucleosis, lymphadenopathy, leukopenia, jaundice with hepatitis, and exanthematous skin eruptions which may progress to exfoliative dermatitis, toxic epidermal necrolysis, or Stevens-Johnson syndrome. Although patients usually improve if Dapsone is withdrawn, fatalities have occurred. Fixed drug eruptions occur in dark-skinned people. Although agranulocytosis has been reported rarely for Dapsone when used alone, reports have been more common when the drug has been used with other agents in the prophylaxis of malaria. Other miscellaneous reactions such as peripheral neuropathy, nephrotic syndrome and renal papillary necrosis have been reported.

Reaction States. Leprosy patients receiving effective chemotherapy may suffer episodes of acute or chronic inflammation which are called reactions. Generally, antileprosy chemotherapy should be continued unchanged but these reactions must be adequately treated since they may result in crippling deformity.

Nonlepromatous Lepra or "Reversal" Reactions. Complications may include severe peripheral neuritis with accompanying cutaneous sensory loss and paralysis and may require surgical decompression. In the management of acute neuritis corticosteroids should always be used.

Lepromatous Lepra or Erythema Nododium Lepromatous (ENL) Reactions. Complications may include neuritis, an increase in muscle weakness, lymphadenitis, iridocyclitis, orchitis and more rarely nephritis and large joint arthritis. In the management of these reactions, corticosteroids, and agents to modify the autoimmune reaction are used.

Interactions

Rifampicin has been reported to increase the plasma clearance of Dapsone, and probenecid has been reported to decrease excretion of Dapsone. Administration of Dapsone with chloroquine and/or primaquine may lead to an increase in methaemoglobin in individuals predisposed to methaemoglobinemia. Increased Dapsone and trimethoprim concentration have been reported following concurrent administration in AIDS patients.

Overdosage

In cases of severe overdosage the stomach should be emptied by aspiration and lavage. There is no specific antidote and therefore treatment should be symptomatic, e.g. intravenous methylene blue 1 to 2 mg/kg bodyweight, intravenous ascorbic acid 0.5 to 1g and oxygen for the methaemoglobinaemia plus general supportive measures. The repeated administration of activated charcoal has been reported to increase the elimination rate of Dapsone and its metabolite following overdosage.

Pharmaceutical Precautions

Store below 25°C. Protect from light.

Medicine Classification

Prescription Only Medicine

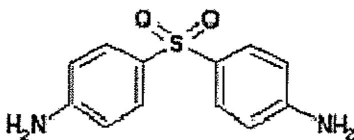
Package Quantities

Dapsone 25mg 100 tablets

Dapsone 100mg 100 tablets.

Further Information

Chemical Name: 4,4'-Sulfonylbisbenzenamine



Formula: $C_{12}H_{12}N_2O_2S$
CAS: 80-08-0
MW: 248.31

List of excipients: Cornstarch, cellulose, magnesium stearate, silicone dioxide

Tablets do not contain alcohol, gluten, lactose, parabens, sugar, sulfilte or tartrazine.

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