

NEW ZEALAND DATA SHEET

1. DAPSONE 25 mg and 100 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 25 mg and 100 mg dapsone.

For full list of excipients, see section 6.1.

Dapsone tablets do not contain alcohol, gluten, lactose, parabens, sugar, sulfite or tartrazine.

3. PHARMACEUTICAL FORM

White, scored tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Dermatitis herpetiformis. Leprosy. Actinomycotic mycetoma.

4.2 Dose and method of 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 100 mg daily, but as little as 50 mg weekly may be adequate. Dosages of up to 300 mg 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 100 mg 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 50 mg 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 600 mg once monthly supervised; Dapsone 100 mg daily, self-administered; Clofazimine 300 mg once monthly, supervised; and 50 mg 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 50 mg or 1 to 2 mg per kg if their body weight is low, can be given.

Paucibacillary leprosy.

Adults: Rifampicin 600 mg 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 50 mg 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 100 mg should be given twice daily and continued for some months after the clinical symptoms have disappeared. Streptomycin at 14 mg/kg daily for the first month and alternate days thereafter (or the equivalent) should always be used in combination with Dapsone. Streptomycin, sulfamethoxazole and trimethoprim is an alternative therapy.

4.3 Contraindications

Hypersensitivity to Dapsone or to any of the excipients listed in section 6.1.

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

4.4 Special warnings and precautions for use

Use with Caution

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

Dapsone should be used with caution in anaemia. Severe anaemia should be treated before starting dapsone.

Routine haematological analysis should be carried out during long-term therapy with sulfones, because the danger of haemolytic anaemia. Patients deficient in glucose-6-phosphate dehydrogenase, or methaemoglobin reductase, or with haemoglobin M are more susceptible to the haemolytic effects of dapsone.

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.

4.5 Interaction with other medicines and other forms of interaction

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 methaemoglobinaemia. Increased Dapsone and trimethoprim concentration have been reported following concurrent administration in HIV/AIDS patients.

4.6 Fertility, pregnancy and lactation

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.

Breast-feeding

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

Dapsone is excreted in breast milk in therapeutic amounts. Sulfones may cause haemolytic anaemia in glucose-6-phosphate deficient neonates.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Most adverse reactions are dose related and uncommon at dosages up to 100 mg 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 methaemoglobinaemia occur in most individuals given more than 200 mg daily. However, there have been case reports of methaemoglobinaemia where the dose was less than 200 mg daily. Dosages up to 100 mg daily are unlikely to cause haemolysis, but individuals with glucose-6-hydrogenase deficiency may be affected by dosages above 50 mg daily (See Section 4.3). Rare reactions include the 'Dapsone syndrome' and hypoalbuminaemia.

The "Dapsone syndrome" is a hypersensitivity reaction, which develops rarely and tends to occur during the first 6 weeks of therapy. It has been suggested that the incidence has increased since the introduction of multidrug therapy for leprosy. Symptoms include rash, which is always present, and may include fever, eosinophilia, mononucleosis, lymphadenopathy, leucopenia, jaundice, and exanthematous skin eruptions. If dapsone is

not stopped immediately, the syndrome may progress to exfoliative dermatitis, hepatitis, albuminuria, psychosis, toxic epidermal necrolysis, or Stevens-Johnson syndrome. Although patients usually improve if Dapsone is withdrawn, fatalities have occurred. Most patients require steroid therapy for several weeks, possibly due to the prolonged elimination time of the drug. 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, anti-leprosy chemotherapy should be continued unchanged but these reactions must be adequately treated since they may result in crippling deformity.

Non-Lepromatous 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 Nodosum 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions

<https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

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 1 g 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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

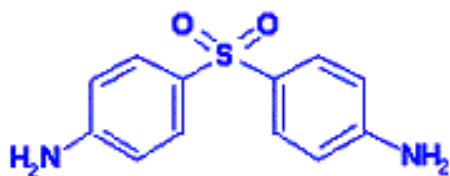
5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterials ATC code: J04BA02

Chemical structure

Chemical Name: 4,4'-Sulfonylbisbenzenamine



Formula: C₁₂H₁₂N₂O₂S

CAS number

80-08-0

MW: 248.31

Mechanism of action

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.

5.2 Pharmacokinetic properties

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

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.

5.3 Preclinical safety data

There are no pre-clinical data available of relevance to the prescriber which are additional to that already included in other sections of the Data Sheet.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Inactive ingredients include:

Cornstarch
Cellulose
Magnesium stearate
Silicone dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

Dapsone 25 mg, 100 tablets in a bottle with a child-resistant cap
Dapsone 100 mg, 100 tablets in a bottle with a child-resistant cap

6.6 Special precautions for disposal

No special requirements.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

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9 DATE OF FIRST APPROVAL

10 May 2005

10 DATE OF REVISION OF THE TEXT

14 September 2020

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
N/A	DS reformatted to align with new requirements
8	Update to New Zealand sponsor address