# 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.

**4.4 Special warnings and precautions for use**

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

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.

The patient should be warned to respond to the presence of clinical signs such as sore throat, fever, pallor, purpura or jaundice. Deaths associated with the administration of dapsone have been reported from agranulocytosis, aplastic anaemia and other blood dyscrasias.

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. This reaction is frequently dose related. Dapsone should be given with caution to these patients or if the patient is exposed

to other agents or conditions such as infection or diabetic ketosis capable of producing haemolysis. Drugs or chemicals which have produced significant haemolysis in G6PD or methaemoglobin reductase deficient patients include dapsone, sulfanilamide, nitrite, aniline, phenylhydrazine, naphthalene, niridazole, nitrofurantoin and 8-amino-antimalarials such as primaquine.
If a significant reduction in leucocytes, platelets or haemopoiesis is noted, dapsone should be discontinued and the patient followed intensively. Folic acid antagonists have similar effects and may increase the incidence of haematologic reactions; if co-administered with dapsone the patients should be monitored more frequently. Patients on weekly pyrimethamine and dapsone have developed agranulocytosis during the second and third month of therapy.

Severe anaemia should be treated prior to initiation of therapy and haemoglobin monitored. Haemolysis and methaemoglobin may be poorly tolerated by patients with severe cardiopulmonary disease.

Cutaneous reactions, especially bullous, include exfoliative dermatitis and are probably one of the most serious, though rare, complications of sulfone therapy. They are directly due to drug sensitisation. Such reactions include toxic erythema, erythema multiforme, toxic epidermal necrolysis, morbilliform and scarlatiniform reactions, urticaria and erythema nodosum. If new or toxic dermatologic reactions occur, sulfone therapy must be promptly discontinued and appropriate therapy instituted.

Leprosy reactional states, (abrupt changes in clinical activity occur in leprosy with any effective treatment and are known as reactional states, see Leprosy Reactional States section under **Section 4.8 Adverse effects (Undesirable effects)** including cutaneous, are not hypersensitivity reactions to dapsone and do not require discontinuation.

Toxic hepatitis and cholestatic jaundice have been reported early in therapy. Hyperbilirubinaemia may occur more often in G6PD deficient patients. When feasible, baseline and subsequent monitoring of liver function is recommended. If abnormal, dapsone should be discontinued until the source of the abnormality is established.

**Paediatric Use:**

Children are treated on the same schedule as adults but with correspondingly smaller doses.

**Use in the elderly**

No data available.

**Effects on laboratory tests**

No data available.

**Use in Porphyria Patients:**
Dapsone has been associated with acute attacks of porphyria and is considered unsafe in patients with porphyria.

**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**:
Rifampicin has been reported to increase the plasma clearance of Dapsone to a level that may compromise efficacy in infections other than leprosy. Increased risk of methaemoglobinaemia from metabolite. Rifampicin concentrations are generally unaffected.

**Probenecid:**
Probenecid has been reported to decrease excretion of Dapsone with a consequent increased risk of adverse effects when given with probenecid, probably as a result of reduced renal excretion of dapsone.

**Chloroquine and Primaquine:**
Administration of Dapsone with chloroquine and/or primaquine may lead to an increase in methaemoglobin in individuals predisposed to methaemoglobinaemia.

**Trimethoprim:**
Increased Dapsone and trimethoprim concentration have been reported following concurrent administration in HIV/AIDS patients and such patients may be at increased risk of dapsone toxicity.

**Amprenavir:**
Possible increase in plasma levels of dapsone.

**Didanosine** (buffered formulations):
Dapsone bioavailability reduced

**Clofazimine:**
Dapsone may antagonise the anti-inflammatory activity of clofazimine.

**Cimetidine:**
Cimetidine has been reported to increase the area under the curve for dapsone, but to decrease the area under the curve for the metabolite dapsone hydroxylamine. Haemotoxicity is thought to be related to production of this metabolite. (See Blood Disorders section under **Section 4.8 Adverse effects (Undesirable effects).**

**Pyrimethamine:**
Folic acid antagonists such as pyrimethamine may increase the likelihood of haematologic reactions.

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

Category B2

The sulfone drugs are generally contraindicated in pregnancy, however, use of Dapsone in pregnant women have not shown that Dapsone increases the risk of fetal abnormalities

when administered during all trimesters of pregnancy or can affect reproduction capacity. 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**

Dapsone should not be used by lactating mothers since it is excreted in substantial amounts in breast milk. Haemolytic reactions can occur in neonates. (**See Section 4.8 Undesirable effects**). A decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

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**

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

**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, leukopenia, 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

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).

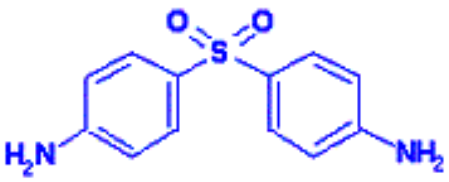
## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterials ATC code: J04BA02

**Chemical structure**

Chemical Name: 4,4'-Sulfonylbisbenzenamine




Formula: $C_{12}H_{12}N_2O_2S$

**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:
Maize starch
Microcrystalline 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

Link Medical Products Pty Ltd
5 Apollo Street
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## 9 DATE OF FIRST APPROVAL

10 May 2005

## 10 DATE OF REVISION OF THE TEXT

22 April 2024

## SUMMARY TABLE OF CHANGES

| Section changed | Summary of new information |
|---|---|
| 8 | NZ address updated |