

## Products: Z400-B and Z400

### **PYRAZINAMIDE**

#### **General information**

A synthetic analogue of nicotinamide that is only weakly bactericidal against *M.tuberculosis*, but has potent sterilizing activity, particularly in the relatively acidic intracellular environment of macrophages and in areas of acute inflammation. It is highly effective during the first two months of treatment while acute inflammatory changes persist and its use has enabled treatment regimens to be shortened and the risk of relapse to be reduced.

It is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout all tissues and fluids. Peak plasma concentrations are attained in two hours and the plasma half-life is about 10 hours. It is metabolised mainly in the liver and is excreted largely in the urine.

#### **Clinical information**

##### **Uses**

A component of all six and eight month anti-TB chemotherapeutic regimens currently recommended by WHO.

##### **Dosage and administration**

*By mouth:*

Adults and children (for the first two or three months)

25 mg/kg daily

35 mg/kg three times weekly

50 mg/kg two times weekly

##### **Contraindications**

- Known hypersensitivity
- Severe hepatic impairment
- Porphyria

##### **Precautions**

- Hepatic impairment (monitor hepatic function)
- Patients with diabetes mellitus (monitored blood glucose--concentrations may change suddenly)
- Gout may be exacerbated.

##### **Use in pregnancy**

Although the safety of pyrazinamide in pregnancy has not been established, the six month regimen based upon isoniazid, rifampicin and pyrazinamide should be used whenever possible.

##### **Adverse effects**

Pyrazinamide is usually well tolerated. Hypersensitivity reactions are rare, but some patients complain of slight flushing of the skin.

Moderate rises in serum transaminase concentrations are common during the early phases of treatment. Severe hepatotoxicity is rare.

As a result of inhibition of renal tubular secretion, a degree of hyperuricaemia usually occurs, but this is often asymptomatic. Gout requiring treatment with allopurinol occasionally develops. Arthralgia, particularly of the shoulders, commonly occurs and is responsive to simple analgesics. Both hyperuricaemia and arthralgia may be reduced by prescribing regimens with intermittent administration of pyrazinamide.

Note: Patients and their care-givers should be told how to recognise signs of liver disorder, and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, vomiting, malaise or jaundice develop.

### **Overdosage**

Little had been recorded on the management of pyrazinamide overdose. Acute liver damage and hyperuricaemia have been reported. Treatment is essentially symptomatic. Emesis and gastric lavage may be of value if undertaken within a few hours of ingestion. There is no specific antidote and treatment is supportive.

### **Storage**

Tablets should be stored in tightly closed containers, protected from light.