Pyrazinamide

Antibiotic Class:
Pyrazinoic acid amide (carboxyamide-2-pyrazine)

Antimicrobial Spectrum:
Narrow spectrum of activity - chiefly *M. tuberculosis*

Mechanism of Action:
Converted to pyrazinoic acid, with (a) acts to acidify the interior of *M. tuberculosis* and (b) may disrupt the function of fatty acid synthase (FAS) type I.

Pharmacodynamics:
Pyrazinamide is very difficult to test *in vitro*, as its activity requires a low pH, which in turn degrades the growth characteristics of *M. tuberculosis.* Pyrazinamide appears to show concentration-dependent activity and concentration-dependent liver toxicity.

Pharmacokinetics:
Cmax: 20-50 mg/L with daily doses, up to 90 mg/L with larger twice-weekly doses; Tmax: about 2 hours; Bioavailability: not known, but likely is high; Protein binding: estimated to be low.

Adverse Effects:
Gastrointestinal intolerance may occur- nausea is common and vomiting may occur. Arthralgias are common. Hepatocellular injury is possible, and appears to be dose-related (large daily dose of 50 mg per kg – no longer used – frequently caused liver enzyme elevation). The 2 drug combination of pyrazinamide and rifampin for latent TB infection (LTBI) is no longer recommended because of hepatotoxicity.

Dosage:
PO: 500 mg tablets

Usual dose: 25 mg/kg once daily, or 50 mg/kg 2-3 times weekly.

Disease state based dosing:

Hepatic failures: Pyrazinamide is usually avoided to prevent further liver damage.

Renal failures: Give 25 mg/kg 3 times weekly, rather than daily.

Contraindications/Warnings/Precautions: Use with caution pregnant women, although data to date are encouraging.

Drug Interactions:
No known interactions based on clearance.

Pregnancy:
Use with caution as indicated.

Monitoring Requirements:
Toxic: baseline liver enzymes, with periodic testing during treatment.