Isoniazid

Antibiotic Class:
Isonicotinic acid hydrazide

Antimicrobial Spectrum:
Isoniazid is highly specific in that it is active only against mycobacteria.

Mechanism of Action:
Although the mechanism of action of isoniazid is not fully understood, it appears to act by inhibiting mycolic acid synthesis, which results in loss of acid fastness and disruption of the cell wall.

Pharmacodynamics:
Based on clinical data, the AUC/MIC appears to be the most predictive PD parameter.

Pharmacokinetics:
Cmax: 3-5 mg/L for 300 mg dose, 9-15 mcg/ml for 900 mg dose; Tmax: 1-2 hours; Bioavailability: over 90%; Protein binding: 10%.

Adverse Effects:
Hepatic: hepatotoxicity, jaundice, hepatitis
Neurotoxicity: Isoniazid causes pyridoxine (vitamin B6) deficiency, leading to peripheral or central neuropathies.
Musculo-skeletal: arthralgias, drug-induced lupus syndrome
Skin: Rash

Dosage:
PO: 100 and 300 mg tablets
IM or IV: 300 mg for injection (IV can be given in 25 ml of normal saline over 5 minutes)

Typical daily dose of isoniazid is 300 mg.
Typical twice or 3 times weekly dose of isoniazid is 900 mg.

Disease state based dosing:
Hepatic failures: No specific recommendations, however, half-life may be prolonged in patients with hepatic insufficiency
Renal failures: No adjustment necessary in most patients.

Contraindications/Warnings/Precautions: Precautions: Hepatic impairment

Drug Interactions:
Isoniazid can block the metabolism of phenytoin and carbamazepine, leading to increased concentrations and potential toxicity.

Pregnancy:
Category A: No evidence of risk in humans. Note that in some case series, post-partum women may be at greater risk of hepatotoxicity.

Monitoring Requirements:
Toxic: baseline liver function tests, bilirubin, serum creatinine, complete blood count and platelet count. Repeat liver function tests particularly in patients over 35 years of age.

Brand names/Manufacturer: Isoniazid (various, including Nydrazid, Sandoz)