Metronidazole

Antibiotic Class:
Nitroimidazole

Antimicrobial Spectrum:
Anaerobic Gram-negative bacilli: *Bacteroides fragilis, Bacteroides species, Fusobacterium spp.*, *Porphyromonas spp.*, *Prevotella spp.*.
Anaerobic Gram-positive bacilli: *Clostridium spp.*
Anaerobic cocci: Peptostreptococcus species, Veillonella species
Protozoa: *Blastocystis hominis, Entamoeba histolytica, Giardia lamblia, Trichomonas vaginalis*

Mechanism of Action:
Exerts action on susceptible organisms in four successive stages: entry of the drug into the organism, its reductive activation, interaction of the reduced intermediate products with intracellular targets, and breakdown of the toxic intermediate products.

Pharmacodynamics:
Metronidazole produces concentration-dependent killing

Pharmacokinetics:
Half-life: 8h (mean); Volume of distribution: 0.51 to 1.1L/kg (adults); Renal clearance: 8-12ml/min; Bioavailability: Approximately 100% PO

Adverse Effects:
Gastrointestinal: abdominal discomfort, anorexia, nausea, vomiting, metallic taste, glossitis, hepatitis (rare), pancreatitis (rare)
Neurologic: peripheral neuropathy, numbness, paraesthesia, ataxia, confusion, encephalopathy, tremors, seizures
Hematologic: reversible leukopenia, thrombocytopenia
Hypersensitivity: maculopapular rashes, urticaria, pruritus, bronchospasm, serum sickness
Other: Metallic taste

Dosage:
IV: 500mg/100ml solution
PO: 250mg, 500mg tablets, 750mg extended release tablet
Topical: 1% cream, 0.75% gel

Adult dose:
Amebiasis – *Entamoeba histolytica* treatment: 750mg q8h x 10 days
Amebiasis - Liver abscess: 500-750mg q8h x 10 days
Anaerobic bacterial life-threatening infections: 15 mg/kg (1g for most adults), followed 7.5 mg/kg q6h for 14-21 days
Anaerobic bacterial infection (mild/moderate): 500 mg IV q6-8h x 7-10 days
Bacterial vaginosis (non-pregnant women): 500 mg PO q12h x 7 days, or 750mg PO q24h (extended-release tablet) x 7 days; alternative: 2g PO x 1 dose
Bacterial vaginosis (pregnant women): 250mg q8h x 7 days
_Clostridium difficile_-associated diarrhea and colitis: 750mg to 2g per day PO divided q6-q8h for 7-14 days
Giardiasis: 250mg PO q8h x 5-7 days or 2g q24h x 3 days
Nongonococcal urethritis: 2g PO x 1 dose + 7 days erythromycin base or erythromycin ethylsuccinate
Perioperative prophylaxis: 15 mg/kg IV; perioperative re-dosing of 7.5 mg/kg should occur q6h
Prophylaxis in sexual assault victims: 2g PO x 1 dose + IM ceftriaxone + azithromycin
Trichomoniases: 250mg PO q8h or 500 mg PO q12h x 7 days or 2g PO x 1 dose

Pediatric dose:
Anaerobic bacterial infection (loading dose): 15 mg/kg IV infused over 60 minutes
Anaerobic bacterial infection (maintenance – pre-term infants): 7.5 mg/kg IV q24h, starting 48hrs after initial dose
Anaerobic bacterial infection (maintenance-term infants): (1-4 weeks of age) 7.5 mg/kg IV q12 h starting 24hrs after initial dose
Anaerobic bacterial infection (infants and children): maintenance, 30 mg/kg/day IV divided q6h, maximum 4 g/day
Amoebic dysentery: 35-50 mg/kg/day PO divided q8h x 10 days; maximum 750mg per dose
Amoebic liver abscess: 50 mg/kg/day PO divided q8h x 7 days; maximum 750mg per dose
Giardiasis: 15 mg/kg/day divided q8h x 7-10 days; maximum 250mg per dose
Pseudomembranous colitis: 30 mg/kg/day PO divided q6h x 7-10 days
Trichomoniases: 15 mg/kg/day PO divided q8h x 7 days

Disease state based dosing:
Renal failure: Inconclusive. Some tertiary references recommend dose reductions (e.g. 500 mg q12h) in patients with CrCl < 10 mL/min however this is debatable
Hepatic failure: Dose reduction by 50% to avoid drug accumulation and possible toxicity.

**Contraindications/Warnings/Precautions:**
Contraindications: First trimester of pregnancy, Hypersensitivity to metronidazole, or other nitroimidazole derivatives
Precautions:
- CNS disease (possibility of seizures and peripheral neuropathy)
- Severe hepatic disease
- Concomitant anticoagulant therapy
- Concomitant alcoholic beverages (disulfiram effect)
- Evidence or a history of blood dyscrasias

**Drug Interactions:**
Warfarin: increased risk of bleeding
Alcohol: disulfiram-like effect (violent retching, vomiting)
Disulfiram: violent retching, vomiting, may be severe (psychosis, confusion, encephalopathy)
Lithium: increased serum lithium levels (levels should be monitored when coadministered)
Phenobarbital: decreased metronidazole serum concentrations
Rifampin: decreased metronidazole serum concentrations
Tacrolimus: increased tacrolimus serum concentrations (monitor serum tacrolimus level)
Carbamazepine: increased carbamazepine serum concentrations (monitor serum carbamazepine level)
Cyclosporine: increased cyclosporine serum concentrations (monitor serum cyclosporine level)
Phenytoin: increased phenytoin serum concentrations (monitor serum phenytoin level)
Cimetidine: increased metronidazole serum concentrations

**Pregnancy:**
Category B: No evidence of risk in humans but studies inadequate.

**Monitoring Requirements:**
Therapeutic:  WBC count, culture and sensitivities, serum levels, signs and symptoms of infection
Toxic:  Periodic CBC, urinalysis, BUN, SCr, AST and ALT, diarrhea,

**Brand names/Manufacturer:**
Available by many names and manufacturers