**AZATHIOPRINE**

**CLASS:** Immunosuppressant Agent

**INDICATIONS:**
Adjunctive therapy in prevention of rejection of kidney transplants; management of active rheumatoid arthritis (RA)

**AVAILABLE DOSAGE FROM THE HOSPITAL:**
AZATHIOPRINE 50MG TAB
AZATHIOPRINE 50MG VIAL

**TRADE NAMES:**

**DOSAGE:**

- **Dosing: Adult**
  
  **Note:** Patients with intermediate TPMT activity may be at risk for increased myelosuppression; those with low or absent TPMT activity receiving conventional azathioprine doses are at risk for developing severe, life-threatening myelotoxicity. Dosage reductions are recommended for patients with reduced TPMT activity.

  **I.V. dose is equivalent to oral dose** (dosing should be transitioned from I.V. to oral as soon as tolerated):

  **Renal transplantation (treatment usually started the day of transplant, however, has been initiated [rarely] 1-3 days prior to transplant):** Oral, I.V.:
  
  Initial: 3-5 mg/kg/day usually given as a single daily dose, then 1-3 mg/kg/day maintenance

  **Rheumatoid arthritis:** Oral:
  
  Initial: 1 mg/kg/day (50-100 mg) given once daily or divided twice daily for 6-8 weeks; may increase by 0.5 mg/kg every 4 weeks until response or up to 2.5 mg/kg/day; an adequate trial should be a minimum of 12 weeks

  Maintenance dose: Reduce dose by 0.5 mg/kg (~25 mg daily) every 4 weeks until lowest effective dose is reached; optimum duration of therapy not specified; may be discontinued abruptly

  **Crohn’s disease, remission maintenance or reduction of steroid use (unlabeled use):** Oral: 2-3 mg/kg/day (Lichtenstein, 2009)

  **Dermatomyositis/polymyositis, adjunctive management (unlabeled use):** Oral: 50 mg/day in conjunction with prednisone; increase by 50 mg/week to total dose
of 2-3 mg/kg/day (Briemberg, 2003); Note: Onset of beneficial effects may take 3-6 months; however, may be preferred over methotrexate in patients with pulmonary or hepatic toxicity.

**Immune thrombocytopenia (ITP), chronic refractory (unlabeled use):** Oral: Maintenance: 100-200 mg/day (Boruchov, 2007)

**Lupus nephritis, maintenance (unlabeled use):** Oral: Initial: 2 mg/kg/day; may reduce to 1.5 mg/kg/day after 1 month (if proteinuria <1 g/day and serum creatinine stable) (Moroni, 2006) or target dose: 2 mg/kg/day (Hahn, 2012; Houssiau, 2010)

**Ulcerative colitis, remission maintenance or reduction of steroid use (unlabeled use):** Oral: 1.5-2.5 mg/kg/day (Kornbluth, 2010)

**Dosage adjustment for concomitant use with allopurinol:** Reduce azathioprine dose to one-third or one-fourth the usual dose when used concurrently with allopurinol. Patients with low or absent TPMT activity may require further dose reductions or discontinuation.

- **Dosing: Geriatric**
  Refer to adult dosing.

- **Dosing: Renal Impairment**
  No dosage adjustment provided in manufacturer’s labeling; however, the following adjustments have been recommended (Aronoff, 2007):
  
  Clcr >50 mL/minute: No adjustment recommended.
  Clcr 10-50 mL/minute: Administer 75% of normal dose.
  Clcr <10 mL/minute: Administer 50% of normal dose.
  Hemodialysis (dialyzable; ~45% removed in 8 hours): Administer 50% of normal dose; supplement: 0.25 mg/kg
  CRRT: Administer 75% of normal dose

- **Dosing: Hepatic Impairment**
  No dosage adjustment provided in manufacturer’s labeling.

- **Dosing: Adjustment for Toxicity**
  Rapid WBC count decrease, persistently low WBC count, or serious infection: Reduce dose or temporarily withhold treatment.
  Severe toxicity in renal transplantation: May require discontinuation.
  Hepatic sinusoidal obstruction syndrome (SOS; veno-occlusive disease): Permanently discontinue.
COMMON SIDE EFFECT:

Frequency not always defined; dependent upon dose, duration, indication, and concomitant therapy.

Central nervous system: Fever, malaise

Gastrointestinal: Nausea/vomiting (RA 12%), diarrhea

Hematologic: Leukopenia (renal transplant >50%; RA 28%), thrombocytopenia

Hepatic: Alkaline phosphatase increased, bilirubin increased, hepatotoxicity, transaminases increased

Neuromuscular & skeletal: Myalgia

Miscellaneous: Infection (renal transplant 20%; RA <1%; includes bacterial, fungal, protozoal, viral), neoplasia (renal transplant 3% [other than lymphoma], 0.5% [lymphoma])

Postmarketing and/or case reports: Abdominal pain, alopecia, anemia, arthralgia, bleeding, bone marrow suppression, fever, hepatic sinusoidal obstruction syndrome (SOS; veno-occlusive disease), hepatosplenic T-cell lymphoma, hypersensitivity, hypotension, interstitial pneumonitis, lymphoma, macrocytic anemia, negative nitrogen balance, pancreatitis, pancytopenia, rash, skin cancer, steatorrhea, Sweet’s syndrome (acute febrile neutrophilic dermatosis)

PREGNANCY RISK FACTORS: D