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