Azathioprine (ay-zah-thye-oh-prin)

Action
Antimetabolite. Interferes with the production of DNA and RNA by inhibiting purine synthesis. Therapeutic Effects: Suppression of cell-mediated immunity and altered antibody formation.

Pharmacokinetics
Absorption: Readily absorbed after oral administration.
Distribution: Crosses the placenta. Enters breast milk in low concentrations.
Metabolism and Excretion: Metabolized to mercaptopurine, which is further metabolized (one route is by thiopurine methyltransferase [TPMT]) to form an inactive metabolite. Minimal renal excretion of unchanged drug.
Half-life: 3 hr.

TIME/ACTION PROFILE
ROUTE ONSET PEAK DURATION
PO (anti-inflammatory) 6–8 wk 12 wk unknown
IV (immunosuppression) days–wk unknown days–wk

Contraindications/Precautions
Contraindicated in: Hypersensitivity; Concurrent use of mycophenolate; OB: Has been shown to cause fetal harm; Lactation: Appears in breast milk.

Adverse Reactions/Side Effects
EENT: retinopathy.
Resp: pulmonary edema.
GI: anorexia, nausea, vomiting, diarrhea, constipation, abdominal pain.
Derm: alopecia, rash.
Hemat: anemia, leukopenia, pancytopenia, thrombocytopenia.
MS: arthralgia.
Misc: weight gain, infection, fever, flu-like syndrome, oral candidiasis

Interactions
Drug-Drug: Additive myelosuppression with antineoplastics, cyclosporine, and myelosuppressive agents. Allopurinol inhibits the metabolism of azathioprine, increasing toxicity. Dose of azathioprine should be reduced to 25–33% of the usual dose when used with allopurinol. May decrease antibody response to live-virus vaccines and increase risk of adverse reactions.
Drug-Natural Products: Concommitant use with echinacea and melatonin may interfere with immunosuppression.

Route/Dosage
Renal Allograft Rejection Prevention
PO, IV (Adults and Children): 3–5 mg/kg/day initially; maintenance dose 1–3 mg/kg/day.

Rheumatoid Arthritis
PO (Adults and Children): 1 mg/kg/day for 6–8 wk, then 0.5 mg/kg/day q 4 wk until response or up to 2.5 mg/kg/day, does not change as tolerated to target dose of 2–3 mg/kg/day.

Inflammatory Bowel Disease (Crohn’s Disease or Ulcerative Colitis) (unlabeled use)
PO (Adults and Children): 50 mg once daily, may be increased to 100 mg every 1–2 wk as tolerated to target dose of 2–3 mg/kg/day.

Use Cautiously in: Infection, Malabsorption, bone marrow reserve, Previous or concurrent radiation therapy, Other chronic debilitating illnesses, Severe renal impairment (serum creatinine >1.5 mg/dL).

Pregnancy Category D
NURSING IMPLICATIONS

Assessment

● Assess for infection (oral, tonsil, armpit, skin, WBC) during therapy.

● Monitor intake and output and daily weight. Decreased urine output may lead to toxicity with this medication.

● Rheumatoid Arthritis: Assess range of motion, degree of swelling, pain, and strength in affected joints; and ability to perform activities of daily living before and periodically during therapy.

● Lab Find Considerations: Monitor renal, hepatic, and hematologic functions before beginning therapy, weekly during the 1st mo, bimonthly for the next 2–3 mo, and monthly thereafter.

● Leukocyte count of <3,000 or platelet count of <100,000/mm³ may necessitate a reduction in dose or temporary discontinuation.

● p in hemoglobin may indicate bone marrow suppression.

● Hepatotoxicity may be manifested by alkaline phosphatase, bilirubin, AST, ALT, and amylase concentrations. Usually occurs within 6 mo of transplant, rarely with rheumatoid arthritis, and is reversible on discontinuation of azathioprine.

● May p serum and urine uric acid and plasma albumin.

Potential Nursing Diagnoses

Risk for infection (Indications)

Implementation

● Do not confuse azathioprine with azacitidine.

● Protect transplant patients from staff members and visitors who may carry infection. Maintain protective isolation as indicated.

● PO: May be administered with or after meals or in divided doses to minimize nausea.

IV Administration

● pH: 5.4.

● IV: Reconstitute 100 mg with 10 mL of sterile water for injection. Swirl gently and mix until dissolved. Reconstituted solution may be administered up to 24 hr after preparation.

● Prepare solution in a biologic cabinet. Wear gloves, mask while handling medication. Discard equipment in specially designated containers.

● Y-Site Compatibility: alfentanil, atracurium, atropine, bevantolin, calcium gluconate, cefazolin, cefuroxime, chloramphenicol, cimetidine, chlorambucil, chlorpromazine, cyclosporine, cyclophosphamide, dexamethasone, diazepam, digoxin, diphenhydramine, dipyrone, dopamine, doxorubicin, doxycycline, enalaprilat, epinephrine, erythromycin, estimates, fentanyl, fluconazole, folic acid, furosemide, gentamicin, heparin, insulin, kaolin, lorazepam, metoclopramide, metoprolol, nalbuphine, nitroprusside, norepinephrine, ondansetron, papaverine, pentobarbital, phenobarbital, phenylephrine, phenytoin, procainamide, prochlorperazine, promethazine, pyridoxine, rocuronium, sodium bicarbonate, streptomycin, succinylcholine, tolbutamide, tocainide, tocopheryl, uracil, vancomycin, vecuronium, verapamil.

● Y-Site Incompatibility: amikacin, ampicillin/sulbactam, ascorbic acid, aztreonam, bumetanide, buprenorphine, butorphanol, calcium chloride, cefazolin, cefoperazone, cefotaxime, cefotetan, cefoxitin, ceftazidime, cephalothin, cephalaxin, cefuroxime, chloramphenicol, chlorpromazine, clindamycin, dantrolene, diazepam, diphenhydramine, dipyrone, dopamine, doxorubicin, doxycycline, enalaprilat, epinephrine, ester, furosemide, gentamicin, haloperidol, hydralazine, ibuprofen, interleukin-2, isoproterenol, ketamine, lactobionate, lidocaine, magnesium sulfate, meperidine, metaraminol, methyldopa, methylprednisolone, minocycline, morphine, nafcillin, nalbuphine, nitroprusside, norepinephrine, ondansetron, papaverine, pentamidine, pentazocine, phenobarbital, phenytoin, procainamide, prochlorperazine, promethazine, pyridoxine, rocuronium, sodium bicarbonate, streptomycin, succinylcholine, tolbutamide, tocainide, tocopheryl, uracil, vancomycin, vecuronium, verapamil.

Patient/Family Teaching

● Instruct patient to take azathioprine as directed. If a dose is missed on a once-daily regimen, omit dose; if on several-times-a-day regimen, take as soon as possible or double next dose. Consult health care professional if more than 1 dose is missed or if vomiting occurs shortly after dose is taken. Do not discontinue without consulting health care professional.

● Advise patient to report unusual tiredness or weakness; cough or hoarseness; fever or chills; lower back or side pain; painful or difficult urination; severe diarrhea; black, tarry stools; blood in urine; or transplant rejection to health care professional immediately.

● Reinforce the need for lifelong therapy to prevent transplant rejection.

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- Instruct patient to notify health care professional of all Rx or OTC medications, vi- tamin, or herbal products being taken and consult health care professional be- fore taking any new medications or receiving any vaccinations while taking this medication.
- Advise patient to avoid contact with persons with contagious diseases and persons who have recently taken oral polio vaccine or other live viruses.
- This drug may have teratogenic properties. Advise patient to use contraception during and for at least 4 mo after therapy is completed.
- Emphasize the importance of follow-up exams and lab tests.
- Hematopoietic Arthritis: Concurrent therapy with salicylates, NSAIDs, or cortico- steroids may be necessary. Patient should continue physical therapy and adequate rest. Explain that joint damage will not be reversed; goals to slow or stop disease process.

Evaluation/Desired Outcomes
- Prevention of transplant rejection.
- Decreased stiffness, pain, and swelling in affected joints in 6–8 wk in rheumatoid arthritis. Therapy is discontinued if no improvement in 12 wk.

Why was this drug prescribed for your patient?