Cincinnati Children's Hospital Medical Center

(6-MP or AZA) with or without Prednisone Treatment Algorithm
Excerpted from Evidence-based care guideline for Management of Pediatric Moderate/Severe Inflammatory Bowel Disease (IBD), Appendix #3; Publication date: 4/5/07

Indications

1. *induction* of remission in children with moderate to severe (per physician global assessment) **CD** AND
   - TPMT genotype consistent with TPMT activity present
   - CBC, ALT, amylase, lipase baseline levels within appropriate limits
2. *induction* of remission in children with moderate to severe **CD** or **UC**
   AND
   - not initially given 6-MP or AZA to induce remission, AND
   - that are steroid-dependent/refractory, defined as:
     - o received more than one course of steroids in one year, or
     - o not achieved remission after one month of prednisone alone, or
     - o not tapered off prednisone after three months OR
   - who have failed or cannot tolerate 5-aminosalcylates (i.e. mesalamine).

3. *maintenance therapy* in children with moderate/severe **CD/UC**

Contraindications

- TPMT genotype that is consistent with absent TPMT activity
- abnormal WBC, ALT, amylase, or lipase levels

See IBD Guideline for more details

Initial Dosing

TPMT level or (genotype) ?

- **Low / (LL)** → Do NOT use 6-MP/AZA
- **Intermediate Activity / (HL)** →
  - Initiate **6-MP** at 0.75-1 mg/kg/d P.O. and if labs OK, advance over 4 wks to 1.5 mg/kg/d ***or***
  - Initiate **AZA** at 1.5 mg/kg/d P.O. and if labs OK, advance over 4 wks to 2.5 mg/kg/d

  AND (when indicated) in combination with Prednisone 1mg/kg P.O. (40-60mg max daily dose)

  Continue for 3 months, if labs normal
- **Normal to High Activity / (HH)** →
  - Initiate **6-MP** at 1.5 mg/kg/d P.O. ***or***
  - Initiate **AZA** at 2.5 mg/kg/d P.O.

  AND (when indicated) in combination with Prednisone 1mg/kg P.O. (40-60mg max daily dose)

  Continue for 3 months, if labs normal

prednisone should be discontinued within 3 months of being initiated

Safety Monitoring

Obtain baseline levels of: WBC, ALT, amylase, lipase

Do Not give live virus vaccines

Repeat ALT and WBC safety monitoring cycle below at 2, 4, 8, 12 wks after initial dosing date and after any dosing changes

ALT normal?
- Yes → **WBC** >3500?
- No → ALT >**10x** normal?
  - Yes →
    - discontinue **6-MP/AZA**,
    - resolve ALT to normal, THEN
    - resume 6-MP/AZA at low dose and advance up to max dose where ALT<3x normal
  - No → ALT >**3x** normal?
    - Yes →
      - decrease **6-MP/AZA** dose by 50%
      - consider drug interactions that may account for hepatotoxicity
    - No → Repeat ALT and WBC safety monitoring cycle

WBC >3500?
- Yes → Repeat ALT and WBC safety monitoring cycle
- No → Consider:
  - decrease **6-MP/AZA** dose 50%, THEN advance dose to max without leukopenia
  - discontinuing 6-MP until leukopenia resolves
  - whether leukopenia is possibly caused by a medication interaction

Efficacy Monitoring

Adequate response to **6-MP/AZA** after 3 months of use? (defined as decreased physician global assessment to Quiescent or Mild)
- Yes → Continue monitoring WBC & ALT every 3 months while on 6-MP/AZA, to check if WBC maintained at >3500 cells/mm^3 and ALT < 3x normal → *Maintenance therapy* for **CD/UC** **6-MP/AZA** P.O. at effective dose
- No → Obtain 6TG level

6TG pmol/8x10^8 erythrocytes level?
- **>400** → Consider therapy options not used yet: Methotrexate or Infliximab
- **<235** →
  - Consider incrementally increasing dose of **6-MP** to max dose of 2.5 mg/kg/d
  - Consider incrementally increasing dose of **AZA** to max dose of 4 mg/kg/d
  - Consider that at same dose of **6-MP/AZA** , 6TG levels may vary widely among patients

→ Repeat safety monitoring with ALT & WBC cycle as above