**TPMT TESTING ALGORITHM**

**Initiation of thiopurine therapy for IBD**

- Has patient had RBC transfusion within past 6 weeks?*
  - NO
  - Is patient a bone marrow transplant recipient?
    - NO
      - TPMT/NUDT15 genotype testing
    - YES
      - Pre-transplant specimen required

**TPMT Metabolite Monitoring**

- TPMT Activity: normal
  - TPMT genotype: normal metabolizer
  - NUDT15 genotype: normal metabolizer
  - Standard dose and monitoring
- TPMT Activity: heterozygote
  - TPMT genotype: intermediate metabolizer
  - NUDT15 genotype: intermediate metabolizer
  - Reduce dose and monitor appropriately
- TPMT Activity: deficient
  - TPMT genotype: poor metabolizer
  - NUDT15 genotype: normal metabolizer
  - Consider alternative medications

**Consider alternative medications***

**Continue therapy and monitoring**

- 6-TGN 235-450 pmol/8x10^8 RBC
- Low/absent 6-TGN and 6-MMP*
- Low 6-TGN and high 6-MMP**
- High 6-TGN and low 6-MMP
- High 6-TGN and 6-MMP

**Dose reduction and close monitoring**

- Refractory; consider alternative medication

**Presence of donor DNA in products may influence genotyping results; however, genotype typically reverts to recipient within 6 weeks after a transfusion.**

**If phenotype testing is preferred, recent research and Mayo Clinic strongly recommend ordering NUDT15 genotype testing in addition. Mayo Clinic Laboratories provides NUDT15 genotyping testing at no additional cost with its TPMT genotyping test (TPNUV).**

**Patients with high TPMT activity cannot achieve therapeutic levels with thiopurine drugs and prescribing higher doses may cause hepatotoxicity.**

**Metabolite monitoring assays would not be useful in cases where the patient has an NUDT15 genetic variant.**

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