Ordering Guidance: *TPMT* and *NUDT15* Genotyping

Pharmacogenetic testing of the thiopurine methyltransferase (TPMT) and nudix hydrolase (NUDT15) genes can identify variants that affect a patient's ability to metabolize thiopurine medications. Testing prior to initiating thiopurine therapy can help prevent severe, potentially fatal, myelosuppressive adverse drug reactions in patients with functionally relevant variants. In Ontario, *TPMT* and *NUDT15* are tested together, as both are critical for predicting thiopurine toxicity across diverse ancestries. For full guidance, see: ontariohealth.ca/clinical/genetics/guidance and filter for pharmacogenomics.

Testing is recommended for all patients prior to initiating thiopurine therapy OR **patients already taking a thiopurine who are not tolerating it well.** Testing is **not** intended for patients who are already taking a thiopurine and tolerating it well, however, testing may be beneficial prior to a planned dose increase.

This testing guidance is relevant for clinicians who prescribe thiopurine medications including:

- azathioprine (e.g., Imuran)
- 6-mercaptopurine (e.g., Purinethol)
- thioguanine (e.g., Lanvis)

These are often prescribed for the Indications below:

- Acute lymphoblastic or promyelocytic leukemias (ALL/APL)
- Ulcerative colitis
- Crohn's disease
- Rheumatoid arthritis
- Solid organ transplant
- Inflammatory or autoimmune skin, liver, lung conditions

To find testing laboratories and requisitions, see the Ontario Genetic Test Directory. This testing is publicly funded, so there is no cost to the patient.

Expected turnaround time: 14 days (from sample collection)

Additional published resources include:

- CPIC guidance on *TPMT* and *NUDT15* testing and management (clinpgx.org/guideline/PA166251442) along with supplemental resources (Most recently updated in 2025 [PMID: 41618934])
- Consensus recommendations on *TPMT* and *NUDT15* Genotyping (2022) (PMCID: PMC9808500)

Still have questions? Consider consulting with your hospital site's clinical pharmacologist or pharmacology department with specific questions, including clinical management, after consulting the published guidance. Alternatively, access the Ontario eConsult Service and navigate to the relevant clinician or specialty group to request a consult. For general assistance navigating genetic services contact a genetic counsellor through gcConnect (1-844-564-4363 or gcConnect@ontariohealth.ca). Do not share PHI with gcConnect.