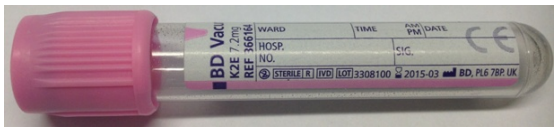
TPMT (Thiopurine Methyl Transferase)

Synonyms	
Clinical Indication	Thiopurine drugs such as azathioprine, 6-mercaptopurine and thioguanine are converted in vivo to form cytotoxic thionucleotides which exert an immunosuppressive effect). TPMT provides the major catabolic pathway for these drugs. If the enzyme is absent in the patient there will be an 'over-dosing' effect, frequently resulting in severe bone marrow depression. TPMT deficiency is polymorphic in the population with 1:250 to 1:300 patients being completely deficient. Genetic carriers of TPMT deficiency occur in 10 to 12% of the population and these carriers have approximately 50% enzyme activity. If treated with normal thiopurine doses, TPMT carrier patients have an increased risk of side effects including nausea and neutropaenia, but will tolerate reduced dose therapy. Prospective measurement of TPMT provides a rational basis for deciding on levels of thiopurine drug therapy. Investigation will normally only be undertaken if patient is about to commence therapy. Repeat requests will not be undertaken unless agreed with the Consultant Biochemist.
Part of Profile / See Also	
Request Form	Combined Pathology manual Blood form or ICE request
Availability / Frequency of Analysis	Referred test: Analysed by King's College Hospital (Synnovis 9093), if specific criteria met.
Turnaround Time	2 weeks
Patient Preparation	Recent blood transfusions will confuse the enzyme phenotype. TPMT is inducible so the analysis should be done before commencing therapy. If the patient is already receiving azathioprine, this must be stated on the request form. Patients should be advised that DNA confirmation may be performed. The only known implication for the genetic variation in TPMT expression is intolerance to thiopurine drugs (see labtestsonline.org.uk for further information).
Sample Requirements	
Specimen Type	Whole blood (EDTA)
Volume	5-10 ml (paediatric 2-5 ml)
Container	 Pink top (EDTA) tube  Paediatric EDTA (Red top – Sarstedt)

Paediatric EDTA (Pink top – BD Microtainer)

Reference Range & Units	TPMT deficient <10 pmol/h/mg Hb TPMT carrier 10-25 pmol/h/mg Hb TPMT normal 26-50 pmol/h/mg Hb TPMT high >50 pmol/h/mg Hb
Interferences	Note that genotyping for TPMT deficiency is preferred for patients with renal failure as TPMT inhibitors may accumulate in blood, giving falsely low TPMT results in the carrier and occasionally, completely deficient results. National guidelines state that children and young adults with acute lymphoblastic leukaemia must be genotyped as concordance between genotype and phenotype in these patients is poor.
Interpretation & Clinical Decision Value (if applicable)	**TPMT deficient <10 pmol/h/mg Hb** Erythrocyte TPMT activity is deficient. The probability of azathioprine /mercaptopurine-induced myelosuppression is VERY HIGH. This patient should not be treated with azathioprine or 6-mercaptopurine. **TPMT carrier 10-25 pmol/h/mg Hb** Erythrocyte TPMT activity is in the carrier range. The probability of azathioprine / mercaptopurine-induced myelosuppression, and intolerance (especially nausea) is high at standard doses. This patient may tolerate and respond to a lower dose (dose increment to a target dose of 50% the standard dose). Monitor FBC and LFTs closely. A blood transfusion in the last 3 months may mask complete TPMT deficiency. **TPMT normal 26-50 pmol/h/mg Hb and high >50 pmol/h/mg Hb** Erythrocyte TPMT activity is in the normal range or elevated. A TPMT above the normal range does not indicate a need to alter dosing strategy. The probability of myelosuppression is low, but not excluded as TPMT deficiency is not the only cause. Standard doses of azathioprine /mercaptopurine are appropriate. Monitor FBC and LFT as per usual. A blood transfusion in the last 3 months may mask complete TPMT deficiency.
References	https://www.synnovis.co.uk/our-tests/tpmt-thiopurine-methyltransferase https://bnf.nice.org.uk/drug/azathioprine.html
Test code	TPMT
Lab Handling	Store the whole blood (EDTA) in the referrals rack at 4°C. Sent daily by courier to King's College Hospital. FBC must be run locally before sending sample and the haemoglobin (Hb) result must be provided on the referral form.

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