TPMT(Thiopurine S-methyltransferase)

Description	TPMT is the enzyme responsible for the conversion of thiopurine drugs (azathioprine, mercaptopurine and 6-thioguanine) to their inactive metabolites.
Indication	Assessment of TPMT activity status is recommended prior to commencing thiopurines in order to guide initial dosing and minimise adverse drug reactions like myelosuppression which are associated with reduced TPMT activity. Please refer to the British National Formulary (BNF) for further information on thiopurines.
Additional Info	89% of individuals are homozygous for the wild type TPMT allele, exhibit normal TPMT activities and generally respond well to standard thiopurine doses. A subgroup within the normal distribution exhibit high TPMT activities; although these individuals may not accumulate therapeutic concentrations of active metabolites, increased doses are not recommended due to the potential for hepatotoxicity. 11% of individuals are heterozygous for mutant TPMT alleles, exhibit low TPMT activities and tend to accumulate an excess of toxic metabolites on standard thiopurine doses. Homozygotes for TPMT mutations (0.3% of individuals) have deficient TPMT activity and are at severe risk of life-threatening myelosuppression due to an inability to deactivate cytotoxic metabolites. Alternative therapeutic agents are advisable in individuals with deficient TPMT activity whereas reduced thiopurine doses are usually tolerated in individuals with low TPMT activity. TPMT activity (phenotype) corrolates well with genotype and both predict an individual's response to thiopurine therapy. Phenotyping is advocated as the front-line test. For further information, please refer to: http://www.labtestsonline.org.uk/understanding/analytes/tpmt
Concurrent Tests	As recommended in the BNF, full blood count and liver function tests are usually monitored if patients are commenced on thiopurines. Red cell thioguanine nucleotide measurement is also advisable to assess the concentrations of active drug metabolites being achieved.
Dietary Requirements	N/A.
Interpretation	**Reference intervals:** Normal: 26 – 50 pmol/h/mgHb Carrier: 10 – 25 pmol/h/mgHb Deficient: < 10 pmol/h/mgHb

	Detailed interpretation is provided with the laboratory report. **Factors to consider:** • Blood transfusions in the 3 months prior to sample collection may mask TPMT deficiency. • TPMT activities are corrected for red blood cell indices so caution is advised in patients with anaemia, particularly where the TPMT activity is around the cut-off between the carrier and normal ranges. TPMT genotyping should be considered in such patients. • Other medications can affect thiopurine metabolism so it is important to consider drug interactions. • Low TPMT activity is not the only cause of myelosuppression.
Collection Conditions	2 x 2.7 mL EDTA whole blood samples (5 mL in total) First Class Post. Store samples at 4ºC prior to dispatch (do NOT freeze). Please provide information on recent transfusions on the request form.
Frequency of testing	Prior to commencing thiopurine therapy. Thiopurine treatment can induce TPMT activity so testing is not recommended once treatment has been started.