Thiopurine S-Methyltransferase Activity in Red Blood Cells
TPMT [E.C. 2.1.1.67]

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A PDF copy of this leaflet can be downloaded from our website.
www.cityassays.org.uk

References


6. O’Kane DJ, Weinshilboum RM, Moyer TP. Editorial: Pharmacogenomics and reducing the frequency of adverse drug events. Pharmacogenomics 2003; 4: 1-4

Sending Specimens for Analysis

**Sample requirement:** A 4 ml EDTA blood sample. Lithium heparin samples are also accepted.

- The sample must not have been frozen. If you have to store samples prior to dispatch please keep at 4°C.
- Please send samples by first class post at ambient temperature to the address on the back of this leaflet.

Reference Ranges and Population Studies

Our reference intervals are as follows:

<table>
<thead>
<tr>
<th>TPMT Activity* (nmol/g Hb/hour)</th>
<th>Deficient</th>
<th>Low</th>
<th>Normal</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6 - 24</td>
<td>25 - 55</td>
<td>&gt;55</td>
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* 37°C, pH 7.4 using 6-MTG as substrate

City Hospital TPMT Assay

Our assay uses 6-thioguanine as the substrate and measures the product 6-methylthioguanine using the method of Ford and Berg². A red blood cell lysate is prepared and incubated with substrates and product determined by HPLC. The assay shows within-batch and between batch imprecision of < 5% and has been validated against another UK TPMT service.

Patient Information

Patients should be informed about the TPMT test prior to taking the sample. City Hospital offers a phenotyping assay and on occasions DNA confirmation may also be performed. The only known health implication for the genetic variation in TPMT expression is intolerance to thiopurine drugs. Patients can be directed to the website www.labtestsonline.org.uk for further information.

Non-Genetic Factors Affecting TPMT Activity

- Patients who have received a recent red blood cell transfusion could give misleading results.
- Thiopurine drugs have been shown to induce TPMT and patients already on azathioprine or mercaptopurine may have increased enzyme activity.
- TPMT is relatively stable and we have shown that at room temperature loss of activity is minimal for at least 8 days.

Clinical Use of TPMT

Thiopurines are widely used as immunosuppressants in gastroenterology and dermatology and in the treatment of acute lymphoblastic leukaemia, rheumatoid arthritis and post-transplant. Thiopurine drugs are metabolised by two major pathways by the enzymes xanthine oxidase and Thiopurine S-methyltransferase (TPMT), a cytosolic enzyme that catalyses the S-methylation of thiopurines to inactive metabolites.

TPMT activity exhibits autosomal co-dominant polymorphism. In a Caucasian population approximately 89% have normal enzyme activity, 11% intermediate activity and 0.3% low or non-detectable levels.

Advances in understanding of the metabolism of thiopurines have led to significant changes in prescribing practice and toxicity monitoring. The recent review by Alex Anstey⁷ includes evidence-based recommendations for routine monitoring of patients on azathioprine, including assessment of TPMT activity prior to treatment.

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![TPMT Activity in 1000 individuals using the City Hospital Assay](chart.png)