

References

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Whole Blood 6-Thioguanine Nucleotides (6-TGN)



Vitamins and Gastroenterology
Laboratory

Clinical Biochemistry
City Hospital

Version No. 1.01

Sending Specimens for Analysis

- Sample requirement: EDTA whole blood. Minimum volume 1ml
- The sample must not have been frozen. If you have to store samples prior to dispatch please keep at 4°C.
- Send samples by first class post at ambient temperature to the address on the back of this leaflet. We receive samples on a Saturday.

Essential Patient Details

Please ensure the following patient details are included to aid result interpretation:

- Current thiopurine drug dose and date this commenced
- Patient diagnosis
- TPMT activity can also be undertaken on this sample but must be requested on the form.

Therapeutic Range

235 – 450 pmol 6-TGN/8x10⁸ cells maximum drug efficiency and clinical remission of inflammatory bowel disease.

TGN Pharmacokinetics

Sample timing: 6-TGN have a half-life of several days and so there is no need to take a sample at any special time.

Steady state concentrations of 6-TGN are reached at between 2-4 weeks after a dose

change. We suggest a sample for therapeutic drug monitoring is timed at 4 weeks from the start of treatment or change in dose.

City Hospital 6-TGN Assay

6-TGN are liberated from red blood cells by perchloric acid and hydrolysed back to their parent thiopurine, 6-thioguanine (6-TG). The 6-TG concentration is then measured by HPLC. The assay shows within-batch and between Imprecision of <8%.

Clinical Use of 6-TGN

Thiopurines are used as immunosuppressants. The therapeutic efficacy of thiopurine is achieved through conversion by the enzyme HPRT to active cytotoxic metabolites, mainly 6-thioguanine nucleotides (6-TGN) and incorporation of these false bases into DNA. Accumulation of high levels of 6-TGN is also responsible for the side effects of thiopurine drugs, and has have been associated with leucopenia.⁴

Therapeutic drug monitoring of 6-TGN concentrations can be useful for:

- Treating patients with low TPMT activity
- Non-compliance or treatment with a suboptimal dose
- Failure to respond to standard doses of thiopurine drugs.⁵

Patients with deficient or low thiopurine s-methyltransferase (TPMT) activity shunt 6-mercaptopurine towards increased 6-TGN production. It is therefore strongly advised patient TPMT status is tested prior to commencing thiopurine therapy.

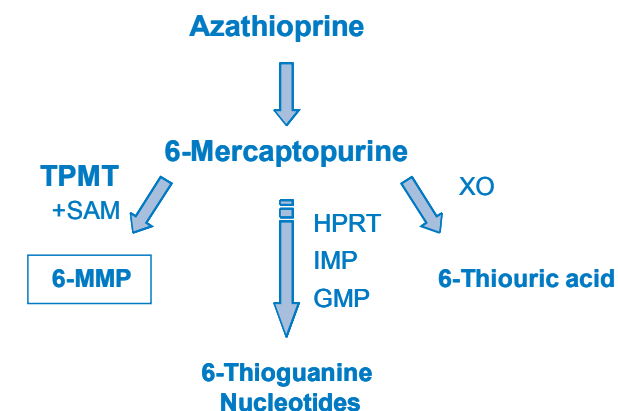


Figure: Thiopurine drug metabolism; azathioprine and 6-mercaptopurine metabolic pathway. [TPMT, Thiopurine S-methyltransferase, SAM, S-adenosyl-L-methionine, XO, Xanthine oxidase, HPRT, Hypoxanthine phosphoribosyltransferase, IMP inosine monophosphate and GMP, guanosine monophosphate].