

## Clinical implications

Thiopurine S-methyltransferase (TPMT) is an essential enzyme for biodegradation of thiopurines. Antitumor drugs thioguanine and mercaptopurine, related to thiopurines, are used especially in hematooncology. Another thiopurine, azathioprine, is an immunosuppressive agent intended for the treatment of autoimmune diseases and prevention of transplant rejection. The thiopurine drug side effects include neurotoxicity, hepatotoxicity, myelosuppression, mucositis and others. The biotransformation activity of the TPMT enzyme may be reduced due to the presence of the single nucleotide polymorphisms in the coding region of the TPMT gene. The most studied deficient alleles are TPMT\*, TPMT\*3A, TPMT\*3B and TPMT\*3C. Limited thiopurine biotransformation leads to the escalation of side effects of treatment. Upon detection of heterozygote it is recommended to reduce the dose of

the drug to 30-70%, in the case of the homozygote and the composite heterozygote it is better to choose an alternative treatment.

## Principle of detection

The kit is intended for detection of TPMT\*2, TPMT\*3A, TPMT\*3B and TPMT\*3C in TPMT gene in human genomic DNA by real-time PCR method (allelic discrimination). The kit allows the determination of haplotypes TPMT\*2, TPMT\*3A, TPMT\*3B and TPMT\*3C in homozygous or heterozygous form. The kit does not distinguish genotype \*1/\*3A (two mutations in cis form) from \*3B/\*3C (the incidence of the composite heterozygote \*3B/\*3C is unlikely in Caucasians).

## Available products








Cat. No.	Product	rxn
3217-025	gb PHARM TPMT	25
3217-050	gb PHARM TPMT	50

1 kit contains reagents to provide 25 or 50 PCR reactions (20 µl volume of each reaction).

## Parameters of the diagnostic kit

- *in vitro* diagnostics
- CE IVD marked
- ready-to-use assay
- sample concentration 10-100 ng/µl
- positive and negative controls included
- FAM and HEX channels detection
- identical amplification profile as gb HEMO, gb GENETIC, gb PHARM kits

## Content of the diagnostic kit

* Component	Conc.	Purpose
 Assay qPCR TPMT*2	1.25×	Detection assay
 Assay qPCR TPMT*3B	1.25×	Detection assay
 Assay qPCR TPMT*3C	1.25×	Detection assay
 Standard WT TPMT	10 <sup>4</sup> cop/µl	Positive Control
 Standard MUT TPMT	10 <sup>4</sup> cop/µl	Positive Control
 Standard HET TPMT	10 <sup>4</sup> cop/µl	Positive Control
 Deionized Water		Negative Control

\* Lid colour



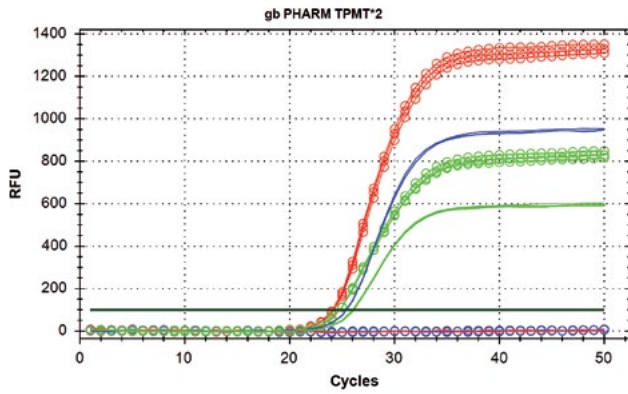


Fig.1 – Detection of TPMT\*2 standards on CFX96 device; blue line – wild type; red line – mutant; green line – heterozygote; smooth line – FAM channel; dotted line – HEX channel

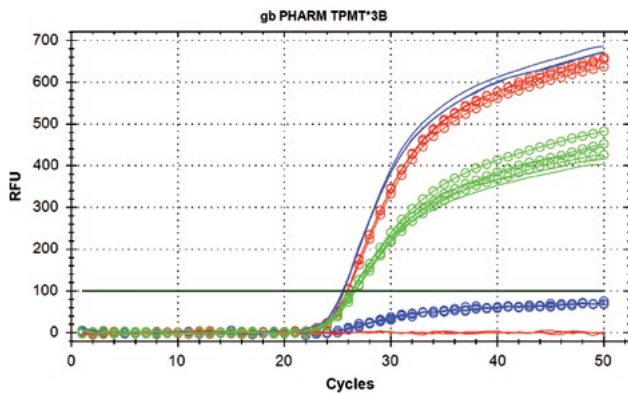


Fig.2 – Detection of TPMT\*3B standards on CFX96 device; blue line – wild type; red line – mutant; green line – heterozygote; smooth line – FAM channel; dotted line – HEX channel

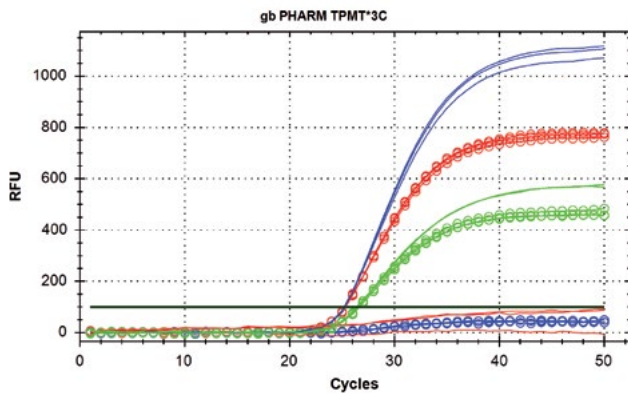


Fig.3 – Detection of TPMT\*3C standards on CFX96 device; blue line – wild type; red line – mutant; green line – heterozygote; smooth line – FAM channel; dotted line – HEX channel

## Validated for cyclers

- Rotor-Gene 3000/6000/Q (Corbett Research, Qiagen)
- iCycler iQ5/CFX96/CFX96 Touch (Bio-Rad)
- ABI 7500/7500 Fast (Applied Biosystems)
- AriaMx (Agilent Technologies)
- MIC (Bio Molecular Systems)
- Light Cycler 480/Cobas z480 (Roche Diagnostics)
- QuantStudio 5 (Applied Biosystems)

