Clinical Pharmacogenetics Implementation Consortium Guidelines for Thiopurine Methyltransferase Genotype and Thiopurine Dosing: 2013 Update

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The Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Thiopurine Methyltransferase Genotype and Thiopurine Dosing was originally published in March 2011. We reviewed recent literature and concluded that although relevant new evidence has been generated, none of the evidence would change the primary dosing recommendations in the original guideline; therefore, the original publication remains clinically current. Up-to-date information on thiopurine methyltransferase (TPMT) gene alleles and nomenclature can be found at PharmGKB (http://www.pharmgkb.org).

The CPIC of the Pharmacogenomics Research Network (http://www.pgrn.org) and the Pharmacogenomics Knowledge Base (PharmGKB, http://www.pharmgkb.org) provides peer-reviewed, updated, evidence-based, freely accessible guidelines for the translation of genetic laboratory tests into actionable prescribing recommendations for specific drugs.1 CPIC guidelines undergo continuous peer review, and information pertaining to gene-specific alleles and nomenclature is updated periodically on the PharmGKB website. Furthermore, approximately every 2 years, each published guideline and associated Supplementary Data online are reviewed and updated accordingly.

The first guideline to be reviewed is the CPIC Guideline for Thiopurine Methyltransferase Genotype and Thiopurine Dosing originally published in March 2011.2 We have done a focused review of the literature between June 2010 and November 2012 on TPMT genotype and thiopurine use (see Supplementary Data, Tables S1–S5, and Figure S1 online). At this time, there is no new evidence that would change our original recommendations in the published guideline; therefore, the original guideline publication remains current.

Since the first CPIC guideline was published, the CPIC Steering Committee has recommended that authors address doses in pediatrics or, at a minimum, comment that there is not enough supporting evidence to allow therapeutic recommendations in pediatrics. As thiopurines are a staple of childhood acute lymphoblastic leukemia and inflammatory bowel disease treatment regimens, much of the evidence (summarized in Supplementary Table S5 online) used to support the original dosing recommendation was generated in children. Furthermore, the dosing recommendations in Table 2 of the main guideline are presented in units of mg/m² and mg/kg. Therefore, our original guideline dosing recommendations can be used in both the adult and pediatric populations.

Although we are not modifying the original main guideline, we have updated the Supplementary Data online to include additional studies that further support our original recommendations (see Supplementary Table S5 online and the Other Considerations subsection of the Supplementary Data online).3–5 In addition, we have added information for additional variant alleles not included in the original guideline (see Supplementary Tables S1 and S2 online).

Up-to-date information on TPMT gene alleles and nomenclature can be found at PharmGKB (http://www.pharmgkb.org).

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CONFLICT OF INTEREST
M.V.R. and W.E.E. receive income from St. Jude for licensing patent rights for TPMT and GGH polymorphisms. They also receive funding for investigator-initiated research on the pharmacology of asparaginase from Sigma-Tau Pharmaceuticals.

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