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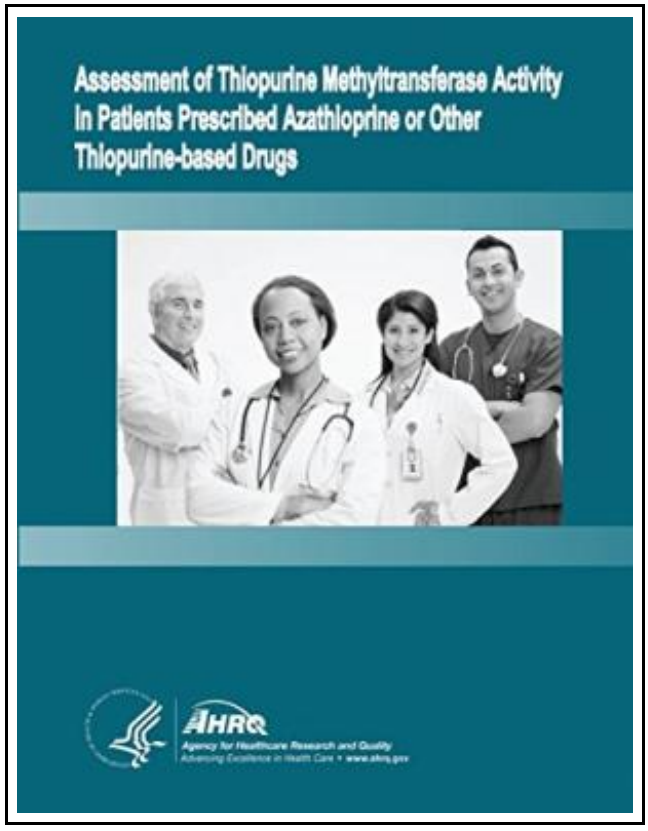

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ASSESSMENT OF THIOPURINE METHYLTRANSFERASE ACTIVITY IN PATIENTS PRESCRIBED AZATHIOPRINE OR OTHER THIOPURINE-BASED DRUGS: EVIDENCE REPORTTECHNOLOGY ASSESSMENT NUMBER 196

Createspace. Paperback. Book Condition: New. This item is printed on demand. Paperback. 288 pages. Dimensions: 11.0in. x 8.5in. x 0.7in.Thiopurine drugs are used to treat chronic autoimmune inflammatory conditions and hematological malignancies, and to prevent organ transplant rejection. The present study focuses on populations with autoimmune disease. Thiopurine drugs are associated with various toxic adverse effects, including myelosuppression, hepatotoxicity, pancreatitis, and flu-like symptoms. The most extensively characterized enzyme in the metabolism of thiopurines is thiopurine methyltransferase (TPMT). TPMT inactivates the active forms of two commonly used thiopurine drugs, azathioprine (AZA) and 6-mercaptopurine (6-MP), by methylation. Multiple studies have shown that lower TPMT enzymatic activity is correlated with higher levels of the active drug metabolites and increased thiopurine toxicity. Genetic polymorphisms associated with lower TPMT enzymatic activity are similarly correlated. Approximately 0. 3 of the population with chronic autoimmune disease that could potentially benefit from thiopurine treatment is homozygous for a variant TPMT allele expressed as low or even absent TPMT activity. These patients are at greatest risk of myelosuppression. Various clinical guidelines recommend measuring TPMT enzymatic activity or screening for TPMT alleles before starting patients on thiopurine drugs. However, the evidence base for these recommendations is unclear. As such, there is a need to review the current literature regarding the assessment of TPMT status prior to administration of thiopurine drugs, to determine if pretreatment TPMT testing reduces drug-related toxicity. This report was commissioned by the Agency for Healthcare Research and Quality to address the following of questions about TPMT genotypic and phenotypic testing methodology, their comparative diagnostic accuracy, effectiveness of pretreatment testing, association with drug toxicity, and costs involved. KQ1. In terms of the analytical performance characteristics of enzymatic measurement of TPMT activity and determination of TPMT allelic polymorphisms: a) What are the preanalytical requirements for enzymatic measurement of TPMT...

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