

	<i>Metabolite Markers of Thiopurines Testing</i>	
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Blue KC reserves the right to review and revise these policies when necessary. When there is an update, we will publish the most current policy to: <https://providers.bluekc.com/ContactUs/PaymentPolicies>.

PROVIDER/ENTITY IMPACTED					
<input checked="" type="checkbox"/> PROFESSIONAL	<input checked="" type="checkbox"/> FACILITY	<input type="checkbox"/> DME	<input type="checkbox"/> AMBULATORY SURGERY	<input checked="" type="checkbox"/> LAB	<input type="checkbox"/> OTHER

LINES OF BUSINESS IMPACTED						
<input checked="" type="checkbox"/> COMMERCIAL	<input checked="" type="checkbox"/> BLUE MEDICARE ADVANTAGE	<input checked="" type="checkbox"/> ACA QHP¹	<input checked="" type="checkbox"/> SMALL GROUP ACA	<input checked="" type="checkbox"/> JAA²	<input checked="" type="checkbox"/> FEP³	<input type="checkbox"/> DENTAL

¹ ACA QHP: Affordable Care Act Qualified Health Plan for Individual/Family ² JAA: Joint Administrative Account ³ FEP: Federal Employee Program

Disclaimer

Blue KC has developed Provider Payment Policies to provide guidance on payment methodologies as they pertain to submitted claims. These policies are written following industry standard recommendations from sources such as:

- Current Procedural Terminology
- Centers for Medicare and Medicaid
- American Medical Association
- National Correct Coding Initiative
- Other professional organizations and societies

Coverage of any service is determined by date of service, a member's eligibility and benefit limits for the service or services rendered, all terms of the Provider Service Agreement, and other standards of coding rules and guidelines.

Final payment is subject to the application of claims adjudication and edits common to the industry.

For confirmation of which services may be eligible for coverage and description of when medical services are considered medically necessary, not medically necessary, or investigational, please contact:

- Blue KC Provider Hotline for Commercial lines of Business 816-395-3929
- Affordable Care Act Provider Hotline 866-859-3822
- Blue Medicare Advantage Provider Hotline 866-508-7140

In the event of a conflict between any policies, the Member's coverage document will govern.

Description/Application

Thiopurines are a class of purine antimetabolite immunomodulators with diverse clinical applications in treatment of autoimmune disorders, transplant rejection, and acute lymphoblastic leukemia (Belmont, 2024). Their therapeutic efficacy, bone marrow toxicity, and liver toxicity have been reported to be related to levels of their downstream metabolites. Due to their complex metabolism, patient response varies considerably between individuals, both in achieving therapeutic drug levels as well as in developing adverse reactions (Bradford & Shih, 2011).

Please note that this policy discusses the monitoring of thiopurine metabolite levels in individuals. For guidance on pharmacogenetic testing prior to therapy, please refer to AHS-M2021 Pharmacogenetic Testing

Policy

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

One-time phenotypic analysis of the enzyme thiopurine methyltransferase (TPMT) **may be reimbursed** for any of the following situations:

- Prior to initiating treatment with azathioprine (AZA), mercaptopurine (6-MP) or thioguanine (6-TG).
- For individuals on thiopurine therapy with abnormal complete blood count (CBC) results that do not respond to dose reduction.

For individuals with inflammatory bowel disease, monitoring of thiopurine metabolite levels **may be reimbursed** for any of the following indications:

- To measure blood levels in individuals suspected of having toxic responses to AZA and/or 6-MP (e.g., hepatotoxicity or myelotoxicity).
- To measure drug levels in individuals who have not responded to therapy (e.g., persistent fever, further weight loss, and bloody diarrhea).

For individuals with acute lymphoblastic leukemia, monitoring of thiopurine metabolite levels **may be reimbursed** for any of the following situations:

- For individuals showing signs of a lack of myelosuppression while on therapy.
- For individuals who do not tolerate thiopurines.
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The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

For all other situations not addressed above, phenotypic analysis of the enzyme TPMT **may not be reimbursed**.

For all other situations not addressed above, analysis of the metabolite markers of azathioprine and 6-mercaptopurine, including 6-methyl-mercaptopurine ribonucleotides (6-MMRP) and 6-thioguanine nucleotides (6-TGN) **may not be reimbursed**.

Coding

CPT	Code Description
80299	Quantitation of therapeutic drug, not elsewhere specified
82657	Enzyme activity in blood cells, cultured cells, or tissue, not elsewhere specified; nonradioactive substrate, each specimen
84433	Thiopurine S-methyltransferase (TPMT)

References and Resources

Avalon Medical Policy AHS – G2115 – Metabolite Markers of Thiopurines Testing

Related Documents

Avalon Medical Policy AHS-M2021 Pharmacogenetic Testing

Revision History

Version	Date	Summary of Revisions
001	07/01/2025	Initial version
002	10/01/2025	Avalon 4 th Quarter updates