Harvard Pilgrim Health Care | TUFTS Health Plan

Point32Health companies

Payment Policy:

Laboratory: Metabolite Markers of Thiopurines Testing

Effective date: Nov. 1, 2025

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products
☐ Tufts Health Plan Commercial products

Public Plans Products

☐ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☐ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☐ Tufts Health RITogether – A Rhode Island Medicaid Plan
☐ Tufts Health One Care – A dual-eligible product

Senior Products

☐ Tufts Health Plan Senior Care Options (SCO) (a dual-eligible product)
☐ Tufts Medicare Preferred HMO/PPO (Medicare Advantage products)

Policy

Thiopurines are a class of purine antimetabolite immunomodulators with diverse clinical applications in treatment of autoimmune disorders, transplant rejection, and acute lymphoblastic leukemia. 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.

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 the Pharmacogenetic Testing policy.

Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

1. One-time phenotypic analysis of the enzyme thiopurine methyltransferase (TPMT) **MEETS COVERAGE CRITERIA** for any of the following situations:
   a. Prior to initiating treatment with azathioprine (AZA), mercaptopurine (6-MP) or thioguanine (6-TG).
   b. For individuals on thiopurine therapy with abnormal complete blood count (CBC) results that do not respond to dose reduction.
2. For individuals with inflammatory bowel disease, monitoring of thiopurine metabolite levels **MEETS COVERAGE CRITERIA** for any of the following indications:
   a. To measure blood levels in individuals suspected of having toxic responses to AZA and/or 6-MP (e.g., hepatotoxicity or myelotoxicity).
   b. To measure drug levels in individuals who have not responded to therapy (e.g., persistent fever, further weight loss, and bloody diarrhea).
3. For individuals with acute lymphoblastic leukemia, monitoring of thiopurine metabolite levels **MEETS COVERAGE CRITERIA** for any of the following situations:
   a. For individuals showing signs of a lack of myelosuppression while on therapy.
   b. For individuals who do not tolerate thiopurines.

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.

4. For all other situations not addressed above, phenotypic analysis of the enzyme TPMT **DOES NOT MEET COVERAGE CRITERIA**.

5. 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), **DOES NOT MEET COVERAGE CRITERIA**.

Applicable CPT/HCPCS Procedure Codes

Procedure codes appearing in policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

Coding

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)

Evidence-based Scientific References

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Publication History

03/01/2026: Annual review; administrative edits
09/01/2025: Policy created to support coverage guidelines, effective for dates of service beginning Nov. 1, 2025

Background and Disclaimer Information

This policy applies to the products of Harvard Pilgrim Health Care and Tufts Health Plan and their affiliates, as identified in the check boxes on the first page for services performed by contracted providers.

Payment is based on member benefits and eligibility on the date of service, medical necessity review, where applicable, and the provider's network participation agreement with the Plan. As every claim is unique, this policy is neither a guarantee of payment, nor a final indication of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization, and utilization management requirements (when applicable), adherence to Plan policies and procedures, and claims editing logic. An authorization is not a guarantee of payment.

Point32Health reserves the right to amend a payment policy at its discretion. CPT and HCPCS codes are updated as applicable; please adhere to the most recent CPT and HCPCS coding guidelines.

We reserve the right to conduct audits on any provider and/or facility to ensure accuracy and compliance with the guidelines stated in this payment policy. If such an audit determines that a provider/facility did not comply with this payment policy, Harvard Pilgrim Health Care and Tufts Health Plan will expect the provider/facility to refund all payments related to noncompliance.