Maple Syrup Urine Disease: Allo-isoleucine and Branched-Chain Amino Acids, Quantitative, Dried Blood Spot

**Test Code:** BMSUD  
**Turnaround time:** 7 days  
**CPT Codes:** 82136 x1

### Condition Description

Maple Syrup Urine Disease (MSUD) is an organic aciduria that is caused by the inability to break down branch-chain amino acids, leucine, isoleucine, and valine. The resulting build-up of these amino acids results in:

- vomiting
- dehydration
- severe metabolic acidosis
- characteristic maple syrup odor of the sweat and urine

MSUD is among the disorders tested for by newborn screening and is treatable by dietary modification. MSUD affects between 1 in 125,000-300,000 people in the general population. MSUD is common in the Old Order Mennonite population of southeastern Pennsylvania, occurring in 1 in 760 live births. MSUD is inherited in an autosomal recessive manner, therefore the recurrence risk for carrier parents of an affected child is 1 in 4.

MSUD is suggested by biochemical analysis of allo-isoleucine and branched chain amino acids, by liquid chromatography - tandem mass spectrometry (LC-MS/MS), or by amino acid analyzer; urine organic acids by gas chromatography/mass spectrometry (GC/MS). MSUD can be diagnosed biochemically by assaying BCKD activity in cultured skin fibroblasts or transformed leukocytes.

MSUD is caused by deficient activity of the branched-chain alpha-keto acid dehydrogenase (BCKD) complex. The BCKD complex consists of three subunits: the 2-oxoisovaleratedehydrogenase alpha subunit (E1 alpha), 2-oxoisovalerate dehydrogenase beta subunit (E1 beta) and lipoamide acyltransferase component (E2). Patients with MSUD may have mutations in the **BCKDHA** (19q13), **BCKDHB** (6p21), or **DBT** gene (1p31), which encode the E1 alpha, E1 beta, and DBT subunits of BCKD complex, respectively.

Dietary monitoring is recommended by plasma amino acids or dried blood spot allo-isoleucine. Please [click here](#) for the GeneReviews summary on MSUD.

### Indications

Second-tier test for patients with abnormal newborn screen results, BCAA elevations, and dietary monitoring of patients with maple syrup urine disease (MSUD).

### Methodology

**Liquid Chromatography-Tandem Mass spectrometry (LC-MS/MS)**  
**Stable Isotope Dilution Analysis**

### Detection

Allo-isoleucine is nearly undetectable in individuals not affected by MSUD. Accordingly, its presence is diagnostic for MSUD, and its absence is sufficient to rule-out classic MSUD.

### Reference Range

Reported in milligrams percent and micromoles. The concentration of leucine is used as monitoring parameter for MSUD patients. The therapeutic range of Leu for MSUD is: 2-6 mg percent.

Reference ranges:  
Allo-isoleucine < 2 umol/L  
Leucine 35 - 215 umol/L  
Isoleucine 13 - 130 umol/L  
Valine 51 - 325 umol/L

### Specimen Requirements

**Type:** Dried Blood Spot

**Specimen Requirements:**  
Peripheral blood from finger prick or heel stick spotted on filter paper, completely saturating the circle. Air dry sample.

**Specimen Collection and Shipping:** Do not expose specimen to heat or direct sunlight. Keep the specimen dry. Ship sample at room temperature with overnight delivery.

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**Special Instructions**

- Do not expose specimen to heat or direct sunlight
- Do not stack wet specimens
- Do not use device or capillary containing EDTA to collect specimen
- Keep the specimen dry

**Related Tests**

- Organic Acids Quantitative Analysis (OA)
- Amino Acids Analysis, Plasma (AA)
- MSUD sequencing (SB) and deletion/duplication (NI)