

## Overview

### Useful For

Diagnosis of molybdenum cofactor deficiency, isolated sulfite oxidase deficiency, and hereditary xanthinuria

Monitoring patients with molybdenum cofactor deficiency or isolated sulfite oxidase deficiency who are on treatment

### Highlights

This test provides a quantitative report of S-sulfocysteine, xanthine, hypoxanthine, and uric acid in urine identified via liquid chromatography-mass spectrometry.

### Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Urine

### Ordering Guidance

This is the recommended test when clinical features are suggestive of, or when molecular testing results suggest, molybdenum cofactor deficiency, isolated sulfite oxidase deficiency, and hereditary xanthinuria. This test includes measurement of relevant purines in addition to urine S-sulfocysteine and uric acid. If the clinical features are suggestive of a purine and pyrimidine metabolism disorder or are nonspecific, order PUPYU / Purine and Pyrimidines Panel, Random, Urine.

**This test will be canceled if ordered with PUPYU.**

### Necessary Information

Patient's age is required.

### Specimen Required

**Supplies:** Urine Tubes, 10 mL (T068)

**Container/Tube:** Plastic, 10-mL urine tube

**Specimen Volume:** 3 mL

**Collection Instructions:** Collect a random urine specimen.

### Forms

[If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request \(T798\)](#) with the specimen.

**Specimen Minimum Volume**

2 mL

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability

**Specimen Stability Information**

| Specimen Type | Temperature | Time    | Special Container |
|---------------|-------------|---------|-------------------|
| Urine         | Frozen      | 90 days |                   |

**Clinical & Interpretive****Clinical Information**

Urine S-sulfocysteine is elevated in 2 disorders with similar clinical phenotypes, molybdenum cofactor deficiency (MoCD) and isolated sulfite oxidase deficiency. Molybdenum is an important trace element that is biosynthesized into an important cofactor, which is essential for the proper functioning of the enzymes, xanthine oxidase, sulfite oxidase, and aldehyde oxidase in addition to nitrogenases and nitrate reductase. Four genes are important in mediating the biosynthetic pathway to create molybdenum cofactor, *MOCS1*, *MOCS2*, *MOCS3*, and *GPHN* (gephyrin). The 3 clinical types of MoCD are autosomal recessive diseases resulting from 2 disease-causing variants in the respective causative gene. MoCDs result in a progressive neurodegenerative disease that manifests with seizures and brain abnormalities in the first weeks to months of life. The most common type of MoCD is MoCD A, caused by variants in *MOCS1* and resulting in neonatal or infantile onset seizures and postnatal encephalopathy with rapidly progressive neurodegeneration. Infants with MoCD B (*MOCS2* or *MOCS3*), and C (*GPHN*) have all been reported but are rare. Infants with MoCD have increased S-sulfocysteine and hypoxanthine and decreased uric acid concentrations in urine. The treatment for MoCD A only is cyclic pyranopterin monophosphate infusion and is most effective when initiated early.

Isolated sulfite oxidase deficiency (ISOD) is an autosomal recessive disorder caused by deficiency of the enzyme sulfite oxidase, which results in progressive neurodegenerative disease in most cases. ISOD is the result of disease-causing variants in the *SUOX* gene. ISOD is a spectrum of disease ranging from severe, early onset disease that appears in the first days of life with seizures, feeding issues, and neurologic issues causing abnormal muscle tone, to mild, later onset disease manifesting after 6 months of age with developmental delay or regression, movement issues, which can be episodic, and ectopia lentis in some cases. Infants with ISOD have increased S-sulfocysteine and normal hypoxanthine concentrations in urine. Treatment is largely symptomatic, with medication for seizures and movement/neurologic issues. Unfortunately, no treatment for the underlying metabolic defect is currently available. Prevalence is unknown, but ISOD is likely underdiagnosed.

Hereditary xanthinuria results in kidney stones and, less commonly, muscle pain and cramping caused by accumulation of xanthine that forms crystals in the kidneys and muscle tissue. There are 2 types of hereditary xanthinuria: type I caused by deficiency of xanthine dehydrogenase resulting from disease-causing variants in the *XDH* gene, and type II caused by deficiency of molybdenum cofactor sulfurase resulting from variants in the *MOCOS* gene. Individuals with xanthinuria have increased xanthine and decreased uric acid concentrations in urine. The incidence of both types of hereditary xanthinuria is about 1 in 69,000 individuals.

## Reference Values

|                 | 0-3 years | 4-6 years | 7-12 years | 13-18 years | >18 years |
|-----------------|-----------|-----------|------------|-------------|-----------|
| Hypoxanthine    | < or =65  | < or =30  | < or =30   | < or =30    | < or =30  |
| Xanthine        | < or =54  | < or =21  | < or =35   | < or =15    | < or =20  |
| Uric Acid       | 350-2500  | 200-2000  | 200-1400   | 150-700     | 70-700    |
| S-Sulfocysteine | < or =11  | < or =5   | < or =5    | < or =5     | < or =5   |

All results reported as mmol/mol creatinine

## Interpretation

Abnormal concentrations of measurable compounds will be reported along with an interpretation. The interpretation of an abnormal metabolite pattern includes an overview of the results and of their significance, a correlation to available clinical information, possible differential diagnosis, recommendations for additional biochemical testing and confirmatory studies (enzyme assay, molecular analysis), name, and phone number of contacts who may provide these studies, and a phone number of the laboratory directors in case the referring physician has additional questions.

## Cautions

Additional confirmatory testing via enzyme assays and molecular genetic testing is required for follow-up of abnormal results.

## Clinical Reference

1. Melcher K, Mountford WK, Hoffmann GF, Ries M. Ultra-orphan diseases: a quantitative analysis of the natural history of molybdenum cofactor deficiency. *Gen Med.* 2015;17(12):965-970
2. Claerhout H, Witters P, Regal L, et al. Isolated sulfite oxidase deficiency. *J Inherit Metab Dis.* 2018;41(1):101-108
3. Misko AL, Liang Y, Kohl JB, Eichler F. Delineating the phenotypic spectrum of sulfite oxidase and molybdenum cofactor deficiency. *Neurol Genet.* 2020;6(4):e486

## Performance

### Method Description

Diluted, filtered urine is mixed with an internal standard mixture and analyzed for hypoxanthine, xanthine, uric acid and S-sulfocysteine by liquid chromatography-tandem mass spectrometry. The ratios of the extracted peak areas of the purine and pyrimidine analytes to the added internal standards are used to calculate the concentration of purines and pyrimidines present in the sample.(la Marca G, Casetta B, Malvagia S, et al. Implementing tandem mass spectrometry as a routine tool for characterizing the complete purine and pyrimidine metabolic profile in urine samples. *J Mass Spectrom.* 2006;41[11]:1442-1452; Rashed MS, Saadallah AAA, Rahbeeni Z, et al. Determination of urinary S-sulphocysteine, xanthine and hypoxanthine by liquid chromatography-electrospray tandem mass spectrometry. *Biomed Chromatogr.* 2005;19[3]:223-230; Monostori P, Klinke G, Hauke J, et al. Extended diagnosis of purine and pyrimidine disorders from urine: LC MS/MS assay development and clinical validation. *PLoS One.* 2019;14[2]:e0212458. doi:10.1371/journal.pone.0212458)

## PDF Report

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No

**Day(s) Performed**

Tuesday, Thursday

**Report Available**

3 to 7 days

**Specimen Retention Time**

1 month

**Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Main Campus

**Fees & Codes****Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

**Test Classification**

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

**CPT Code Information**

82542

**LOINC® Information**

| Test ID | Test Order Name          | Order LOINC® Value |
|---------|--------------------------|--------------------|
| SSCTU   | S-Sulfocysteine Panel, U | 94397-7            |

| Result ID | Test Result Name       | Result LOINC® Value |
|-----------|------------------------|---------------------|
| 607007    | Interpretation (SSCTU) | 59462-2             |
| 607002    | Hypoxanthine           | 38366-1             |
| 607003    | Xanthine               | 38371-1             |
| 607004    | Uric Acid              | 34385-5             |
| 607005    | S-Sulfocysteine        | 33876-4             |
| 607006    | Reviewed By            | 18771-6             |