

Overview

Useful For

Screening patients suspected of having a lysosomal storage disorder

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
CTS02	Ceramide Trihex and Sulfatide, U	Yes, (Order CTSU)	Yes
MPS02	Mucopolysaccharides Quant, U	Yes, (Order MPSQU)	Yes
OLI02	Oligosaccharide Screen, U	Yes, (Order OLIGU)	Yes
BG721	Lysosomal Storage Disorders Interp	No	Yes

Genetics Test Information

This is a general urine screening test for a broad array of lysosomal storage (LSD) and related disorders. Not all LSD are detectable by this method.

Testing Algorithm

For information see:

- [Lysosomal Storage Disorders Diagnostic Algorithm, Part 1](#)
- [Lysosomal Storage Disorders Diagnostic Algorithm, Part 2](#)
- [Lysosomal Storage Disorders Screen Interpretive Algorithm](#)

Special Instructions

- [Fabry Disease Diagnostic Testing Algorithm](#)
- [Biochemical Genetics Patient Information](#)
- [Lysosomal Storage Disorders Diagnostic Algorithm, Part 2](#)
- [Lysosomal Storage Disorders Diagnostic Algorithm, Part 1](#)
- [Lysosomal Storage Disorders Screen Interpretive Algorithm](#)

Highlights

The first step in a diagnostic workup of an individual suspected of having a lysosomal storage disorder (LSD) includes urine analyses for metabolites associated with mucopolysaccharidoses, oligosaccharidoses, disorders of sulfatide degradation, and LSDs with characteristic urine profiles.

This test contains a combined analysis of ceramide trihexosides, mucopolysaccharides, oligosaccharides, and sulfatides. This combined analysis of these disease-specific markers allows for the identification of disorders that may not be picked up using any of the single tests alone.

Method Name

CTS02, OLI02: Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)
MPS02: Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)
BG721: Medical Interpretation

NY State Available

Yes

Specimen**Specimen Type**

Urine

Ordering Guidance

This test is the recommended screening test for the initial workup of a suspected lysosomal storage disorder (LSD) when the patient's clinical features are not suggestive of any specific LSD.

Necessary Information

1. Patient's age is required.
2. [Biochemical Genetics Patient Information](#) (T602) is recommended. This information aids in providing a more thorough interpretation of results. Send information with specimen.

Specimen Required**Patient Preparation:**

1. Do not administer low-molecular weight heparin before specimen collection.
2. Baby wipes or wipes containing soaps or lotions should not be used before specimen collection because these may interfere with results.

Supplies: Urine Tubes, 10 mL (T068)

Container/Tube: Plastic, 10-mL urine tube

Specimen Volume: 10 mL

Pediatric Volume: 3 mL

Collection Instructions: Collect a **first-morning**, random urine specimen.

Forms

1. [Biochemical Genetics Patient Information](#) (T602)
2. [If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request](#) (T798) with the specimen.

Specimen Minimum Volume

3 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	Refrigerated (preferred)	15 days	
	Frozen	365 days	
	Ambient	7 days	

Clinical & Interpretive

Clinical Information

Lysosomal storage disorders (LSD) are a diverse group of inherited diseases characterized by the intracellular accumulation of macromolecules leading to cell damage and organ dysfunction. Approximately 50 LSD have been described with a wide phenotypic spectrum and ranging in severity from neonatal lethal to later onset milder variants.

Although classification is not always straightforward, LSD are generally categorized according to the type of storage material that accumulates in the cells and tissues. Major categories include mucopolysaccharidoses, oligosaccharidoses, mucolipidoses, and sphingolipidoses. In many cases, accumulating analytes can be detected in urine. Screening for these disorders typically begins with an analysis to detect disease-specific metabolite patterns or profiles indicative of a LSD. The combined analysis of disease-specific markers for LSD in multiple tests can allow for the identification of additional disorders that may not be picked up using any of the single tests alone.

Disorders detectable by this approach include the oligosaccharidoses: alpha-mannosidosis, aspartylglucosaminuria, beta-mannosidosis, fucosidosis, Schindler disease, and sialidosis; the sphingolipidoses: GM1 gangliosidosis, Sandhoff disease, galactosialidosis, saposin B deficiency, metachromatic leukodystrophy, multiple sulfatase deficiency, Fabry disease, and Gaucher disease; the mucopolysaccharidoses excluding MPS IX (hyaluronidase deficiency); the glycogen storage disorder Pompe disease and the mucolipidoses types II and III. Additionally, other disorders such as congenital disorder of glycosylation (CDG) type IIb, and deglycosylation disorders such as NGLY1-CDG may also be detected.

The mucopolysaccharidoses (MPS) are a subset of lysosomal storage disorders caused by the deficiency of any one of the enzymes involved in the stepwise degradation of dermatan sulfate, heparan sulfate, keratan sulfate, or chondroitin sulfate (glycosaminoglycans: GAG). Undegraded or partially degraded GAG (also called mucopolysaccharides) are stored in lysosomes and excreted in the urine. Accumulation of GAG in lysosomes interferes with normal functioning of cells, tissues, and organs resulting in the clinical features observed in MPS disorders. There are 11 known enzyme deficiencies that result in MPS. In addition, abnormal GAG storage is observed in multiple sulfatase deficiency and in I-cell disease. Finally, an abnormal excretion of GAG in urine is observed occasionally in other disorders including active bone diseases, connective tissue disease, hypothyroidism, urinary dysfunction, and oligosaccharidoses.

The oligosaccharidoses (glycoproteinoses) are a subset of lysosomal storage disorders caused by the deficiency of any one of the lysosomal enzymes involved in the degradation of complex oligosaccharide chains. They are characterized by the abnormal accumulation of incompletely degraded oligosaccharides in cells and tissues and the corresponding increase of related free oligosaccharides in the urine. Clinical features can include bone abnormalities, coarse facial

features, corneal cloudiness, organomegaly, muscle weakness, hypotonia, developmental delay, and ataxia. Age of onset ranges from early infancy to adult and can even present prenatally.

The sphingolipidoses are a subset of lysosomal storage disorders caused by a defect in any one of the enzymes that degrade complex ceramide containing lipids. They are characterized by the excessive accumulation of sphingolipids in the tissues, particularly in the central nervous system resulting in progressive neurodegeneration and developmental regression. In 2 conditions, Fabry disease and Gaucher disease type I, there is only systemic involvement. In many cases, sphingolipidoses can be detected by through oligosaccharide analysis in urine.

Because of the similarity of features across disorders and their phenotypic variability, clinical diagnosis of LSD can be challenging; therefore, the combined analysis of multiple urine screening tests is an important tool for the initial workup of an individual suspected of having a lysosomal storage disorder. Abnormal results can be followed up with the appropriate enzyme or molecular analysis.

Reference Values

An interpretive report will be provided.

Interpretation

When abnormal results are detected with characteristic patterns, a detailed interpretation is given, including an overview of the results and their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro confirmatory studies (enzyme assay and molecular test).

Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. Specific enzymatic or molecular assays is recommended to confirm positive results.

Cautions

In rare instances, a normal excretion of ceramide trihexosides may be seen in individuals who are carriers of, or affected with, Fabry disease. If Fabry disease is clinically suspected, see [Fabry Disease Testing Algorithm](#) for additional testing recommendations.

Not all lysosomal storage disorders are detectable through urine screening.

Clinical Reference

1. Lysosomal Disorders. In: [Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds.](#) The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed November 30, 2023. Available at <https://ommbid.mhmedical.com/book.aspx?bookID=2709#225069419>
2. Enns GM, Steiner RD, Cowan TM. Lysosomal disorders. In: Sarafoglou K, Hoffmann GF, Roth KS. Pediatric Endocrinology and Inborn Errors of Metabolism. McGraw Hill; 2009
3. Kingma SDA, Bodamer OA, Wijburg FA. Epidemiology and diagnosis of lysosomal storage disorders; challenges of screening. Best Pract Res Clin Endocrinol Metab. 2015;29(2):145-157. doi:10.1016/j.beem.2014.08.004

Performance

Method Description

Ceramide trihexosides and sulfatides are determined by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis. Urine specimens are centrifuged, and all but 50 mL of supernatant is discarded from the pellet. Methanol including internal standards is added, and then ceramide trihexosides and sulfatides are extracted in chloroform. After centrifugation, the bottom chloroform layer is spotted onto a MALDI plate, matrix is added and allowed to air dry. The plate is then analyzed using a MALDI TOF/TOF 5800 Analyzer. (Unpublished Mayo method)

Dermatan sulfate (DS), heparin sulfate (HS), keratan sulfate (KS) and chondroitin-6-sulfate (C6S) are enzymatically digested from urine. The reaction mixture is centrifuged and analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The ratio of the extracted peak area of DS, HS, KS and C6S to internal standard as determined by LC-MS/MS is used to calculate the concentration of DS, HS, KS and C6S in the sample. (Unpublished Mayo method)

Oligosaccharides in urine samples are extracted using Oasis HLB and carbograph columns and lyophilized overnight. Oligosaccharides are permethylated, the tubes centrifuged, and the supernatant removed. The supernatant is quenched with water, neutralized with acetic acid, extracted, eluted, and again lyophilized overnight. Specimens are resuspended, mixed 1:1 with a matrix solution, spotted onto a MALDI plate and allowed to air dry. The plate is then analyzed using a MALDI TOF/TOF 5800 Analyzer. (Xia B, Asif G, Arthur L, et al. Oligosaccharide analysis in urine by MALDI-TOF mass spectrometry for the diagnosis of lysosomal storage diseases. Clin Chem 2013;59[9]:1357-1368, Hall PL, Lam C, Alexander JJ. Urine oligosaccharide screening by MALDI-TOF for the identification of NGLY1 deficiency. Mol Genet Metab. 2018;124[1]:82-86)

PDF Report

No

Day(s) Performed

Varies

Report Available

11 to 17 days

Specimen Retention Time

1 month

Performing Laboratory Location

Rochester

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

83789
83864
84377
82570

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LSDS	Lysosomal Storage Disorders Scrn, U	94423-1

Result ID	Test Result Name	Result LOINC® Value
606773	Lysosomal Storage Disorders Interp	94423-1
606772	Reviewed By	18771-6