MAYO CLINIC LABORATORIES

# Test Definition: HSMP

Hepatosplenomegaly Panel, Plasma

## Overview

### Useful For

As a component to the initial evaluation of a patient presenting with hepatosplenomegaly, using plasma specimens

This test is **not useful for** the identification of carriers.

This test **should not be used** as a monitoring tool for patients with confirmed diagnoses.

### Highlights

This is a screening test for a select number of lysosomal and lipid storage disorders, including cerebrotendinous xanthomatosis, Gaucher disease, and Niemann-Pick disease types A, B (also known as acid sphingomyelinase deficiency), and C.

The above conditions may all have hepatosplenomegaly as a presenting sign, making this test a helpful component of a patient's initial evaluation.

### Method Name

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

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma

### Ordering Guidance

This test **should not be used** for monitoring of patients with confirmed diagnoses. If testing requested is for monitoring purposes, see:
CTXP / Cerebrotendinous Xanthomatosis, Plasma
GPSYP / Glucopsychosine, Plasma
OXNP / Oxysterols, Plasma

### Specimen Required

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)
**Collection Container/Tube:**
**Preferred:** Lavender top (EDTA)
**Acceptable:** Green top (sodium heparin, lithium heparin), yellow top (ACD B)
**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 0.3 mL

**Collection Instructions:**

1. Centrifuge at 4 degrees C, if possible
2. Aliquot plasma into plastic vial. **Do not disturb or transfer the buffy coat layer**.
3. Send frozen

## Forms

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

## Specimen Minimum Volume

0.25 mL

## Reject Due To

| | |
|---|---|
| Gross hemolysis | OK |
| Gross lipemia | OK |
| Gross icterus | OK |

## Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Plasma | Frozen | 65 days | |

## Clinical & Interpretive

### Clinical Information

Hepatosplenomegaly is a presenting or accompanying feature for many different inborn errors of metabolism. It typically is a consequence of chronic hepatic dysfunction or abnormal storage of lipids, sugars, or other improperly metabolized analytes due to a particular enzymatic deficiency. The diagnosis can occasionally be narrowed down by consideration of clinical symptoms; however, clinical diagnosis can be difficult due to similarity of clinical features across disorders as well as phenotypic variability. Therefore, screening tests can play an important role in the workup of a patient presenting with hepatosplenomegaly who may have a lysosomal or lipid storage disorder.

The conditions detected in this assay are cerebrotendinous xanthomatosis, Gaucher disease, and Niemann-Pick disease types A, B (also known as acid sphingomyelinase deficiency), and C.

Patients with abnormal results should have follow-up enzymatic or molecular testing for confirmation of diagnosis.

Table. Conditions Identifiable by Method

| Disorder | Onset | Analyte detected | Gene |
|---|---|---|---|
| Cerebrotendinous xanthomatosis | Infancy-adulthood | 7-Alpha-hydroxy-4-cholesten-3-one (7a-C4)<br>7-Alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4) | *CYP27A1* |

| | | | |
|---|---|---|---|
| | Phenotype: Early onset diarrhea, cataracts, tendon/cerebral xanthomas, osteoporosis, neuropsychological manifestations, liver disease/hepatosplenomegaly. | | |
| Gaucher disease | Type I: childhood/adult<br>Types II/III: neonatal-early childhood | Glucopsychosine | *GBA1* |
| | Phenotype: All types exhibit hepatosplenomegaly and hematological abnormalities.<br>Type I: Organomegaly, thrombocytopenia, and bone pain. Absence of neurologic symptoms.<br>Types II/III: Primary neurologic disease, developmental delay/regression, hepatosplenomegaly, lung disease. Patients with type II typically die by 2 to 4 years of age. Patients with type III may have a less progressive phenotype and may survive into adulthood. | | |
| Niemann-Pick type A/B (NPA/NPB) | NPA: neonatal<br>NPB: birth-adulthood | Lyso-sphingomyelin (LSM)<br>LSM 509 | *SMPD1* |
| | Phenotype:<br>NPA: Feeding difficulties, jaundice, hepatosplenomegaly, neurologic deterioration, lung disease, hearing and vision impairment, cherry red macula, death usually by 3 years of age.<br>NPB: Mainly limited to visceral symptoms; hepatosplenomegaly, stable liver dysfunction, pulmonary compromise, osteopenia. | | |
| Niemann-Pick type C (NPC) | Variable (perinatal-adulthood) | Cholestane-3 beta, 5-alpha, 6-beta-triol<br>LSM 509 | *NPC1 or NPC2* |
| | Phenotype: Variable clinical presentation; ataxia, vertical supranuclear gaze palsy, dystonia, progressive speech deterioration, seizures, +/- hepatosplenomegaly. | | |

## Reference Values

Cholestane -3-beta, 5-alpha, 6-beta-troil
Cutoff: < or =0.070 nmol/mL

7-Ketocholesterol
Cutoff: < or =0.100 nmol/mL

Lyso-sphingomyelin Cutoff: < or =0.100 nmol/mL

Glucopsychosine Cutoff: < or =0.003 nmol/mL

7-Alpha-hydroxy-4-cholesten-3-one Cutoff: < or =0.300 nmol/mL

7-Alpha,12-alpha-dihydroxycholest-4-en-3-one
Cutoff: < or =0.100 nmol/mL

## Interpretation

An elevation of 7-alpha-hydroxy-4-cholesten-3-one (7a-C4) or 7-alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4) or both is strongly suggestive of cerebrotendinous xanthomatosis.

An elevation of glucopsychosine is indicative of Gaucher disease.

An elevation particularly of lyso-sphingomyelin (LSM) is highly suggestive of Niemann-Pick type A or B disease.

An elevation of cholestane-3-beta, 5-alpha, 6-beta-triol is highly suggestive of Niemann-Pick disease type C.

## Cautions

Patients with Wolman disease or cholestatic biliary atresia may have a profile similar to Niemann-Pick disease type C.

Patients with bile acid malabsorption or ileal resection may have elevations of 7-alpha-hydroxy-4-cholesten-3-one (7aC4).

This test does not identify all causes of hepatosplenomegaly.

A positive test result is strongly suggestive of a diagnosis but needs follow-up by stand-alone biochemical or molecular assay.

## Clinical Reference

1. DeBarber AE, Luo J, Star-Weinstock M, et al. A blood test for cerebrotendinous xanthomatosis with potential for disease detection in newborns. J. Lipid Res. 2014;55(1):146-154
2. Federico A, Dotti MT, Gallus GN: Cerebrotendinous xanthomatosis. In: Adam MP, Everman DB, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2003. Updated November 14. 2024. Accessed December 2, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1409/
3. Grabowski GA, Petsko GA, Phil D, Kolodny EH: Gaucher disease. 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 December 2, 2024. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225546056
4. Murugeasan V, Chuan WL, Liu J, et al. Glucosylsphingosine is a key biomarker of Gaucher disease. Am J Hematol. 2016;91(11):1082-1089
5. Wasserstein MP, Schuchman EH. Acid sphingomyelinase deficiency. In: Adam MP, Everman DB, Mirzaa GM, et al., eds. GeneReviews [Internet]. University of Washington, Seattle; 2006. Updated April 27, 2023. Accessed December 2, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1370/
6. Wasserstein M, Dionisi-Vici C, Giugliani R, et al. Recommendations for clinical monitoring of patients with acid sphingomyelinase deficiency (ASMD). Mol Genet Metab. 2019;126(2):98-105. doi:10.1016/j.ymgme.2018.11.014
7. Patterson M: Niemann-Pick disease type C. In: Adam MP, Everman DB, Mirzaa GM,et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2000.Updated December 10, 2020. Accessed December 2, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1296/
8. Geberhiwot T, Moro A, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet J Rare Dis. 2018;13(1):50. Published 2018 Apr 6. doi:10.1186/s13023-018-0785-7

## Performance

### Method Description

An internal standard is added to an aliquot of plasma, which is then subjected to protein precipitation. Following centrifugation, the supernatant is subjected to liquid chromatography tandem mass spectrometry (LC-MS/MS) analysis. The MS/MS is operated in the multiple reaction monitoring positive mode to follow the precursor to product species transitions for each analyte and internal standard. The ratio of the extracted peak areas to internal standard determined by the LC-MS/MS is used to calculate the concentration of in the sample.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Tuesday, Thursday

### Report Available

3 to 7 days

### Specimen Retention Time

2 months

### 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 |
|---|---|---|
| HSMP | Hepatosplenomegaly Panel, P | 92743-4 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 601542 | Interpretation (HSMP) | 59462-2 |
| 601536 | Cholestane-3beta,5alpha,6beta-triol | 92755-8 |
| 601537 | 7-Ketocholesterol | 92764-0 |

| | | |
|---|---|---|
| 601538 | Lyso-sphingomyelin | 92747-5 |
| 601539 | Glucopsychosine | 92750-9 |
| 601540 | 7a-hydroxy-4-cholesten-3-one | 92761-6 |
| 601541 | 7a,12a-dihydroxycholest-4-en-3-one | 92758-2 |
| 601543 | Reviewed By | 18771-6 |