# Test Definition: HSMP

Hepatosplenomegaly Panel, P

## Overview

### Useful For

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

This test is **not suitable 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 diseases types A, B, 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

**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, taking care not to 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.

## Reject Due To

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

## Specimen Minimum Volume

0.25 mL

## Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Plasma | Frozen (preferred) | 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, 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 | Incidence |
|---|---|---|---|---|
| Cerebrotendinous xanthomatosis (CTX) | Infancy-adulthood | 7-Alpha-hydroxy-4-cholesten-3-one (7a-C4)<br><br>7-alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4) | *CYP27A1* | 1 in 50,000<br><br>As high as 1 in 400 in Druze population. |
| | Phenotype: early onset diarrhea, cataracts, tendon/cerebral xanthomas, osteoporosis, neuropsychological manifestations, liver disease/hepatosplenomegaly. | | | |
| Gaucher disease | Type I: childhood/adult<br><br>Types II/III: neonatal-early childhood | Glucopsychosine (GPSY) | *GBA* | Type I:<br><br>1 in 30,000 to 1 in 100,000<br><br>Types II/III:<br><br>1 in 100,000 |
| | Phenotype: all types exhibit hepatosplenomegaly and hematological abnormalities.<br><br>Type I: organomegaly, thrombocytopenia, and bone pain. Absence of neurologic symptoms.<br><br>Types II/III: primary neurologic disease, developmental delay/regression, hepatosplenomegaly, lung disease. Patients with Type II typically die by age 2 to 4. Patients with Type 3 may have a less progressive phenotype and may survive into | | | |

| | | | | |
|---|---|---|---|---|
| Niemann-Pick type<br><br>A/B (NPA/NPB) | NPA: neonatal<br><br>NPB: birth-adulthood | Lyso-sphingomyelin (LSM)<br><br>lyso-sphingomyelin 509 (LSM 509) | *SMPD1* | Combined incidence<br><br>1 in 250,000 |
| | Phenotype:<br><br>NPA: feeding difficulties, jaundice, hepatosplenomegaly, neurologic deterioration, lung disease, hearing and vision impairment, cherry red macula, death usually by age 3.<br><br>NPB: mainly limited to visceral symptoms; hepatosplenomegaly, stable liver dysfunction, pulmonary compromise, osteopenia. | | | |
| Niemann-Pick type C (NPC) | Variable<br><br>(perinatal-adulthood) | Cholestane-3 beta, 5-alpha, 6-beta-triol (COT)<br><br>lyso-sphingomyelin 509 (LSM 509) | *NPC1 or NPC2* | 1 in 120,000 to 1 in 150,000 |
| | Phenotype: Variable clinical presentation. Ataxia, vertical supranuclear gaze palsy, dystonia, progressive speech deterioration, seizures, +/- hepatosplenomegaly. | | | |

Patients with testing indicative of one of the above disorders should have follow-up enzymatic of molecular testing for confirmation of diagnosis.

## Reference Values

CHOLESTANE-3-BETA, 5-ALPHA, 6-BETA-TRIOL

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 (7a-C4)

Cutoff: < or =0.300 nmol/mL

7-ALPHA,12-ALPHA-DIHYDROXYCHOLEST-4-en-3-ONE (7a12aC4)

Cutoff: < or =0.100 nmol/mL

### Interpretation

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

An elevation of glucopsychosine (GPSY) is indicative of Gaucher disease.

An elevation of lyso-sphingomyelin (LSM) and lyso-sphingomyelin 509 (LSM 509) is highly suggestive of Niemann-Pick type A or B (NPA or NPB) disease.

An elevation of cholestane-3-beta, 5-alpha, 6-beta-triol (COT) lyso-sphingomyelin 509 (LSM 509) is highly suggestive of Niemann-Pick disease type C (NPC).

### Cautions

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

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 Jan;55(1):146-154

2. Federico A, Dotti MT, Gallus GN: Cerebrotendinous xanthomatosis. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2003. Updated April 14, 2016. Accessed November 20, 2020. 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 February 4, 2021. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546056&bookid=2709

4. Murugeasan V, Chuan WL, Liu J, et al: Glucosylsphingosine is a key biomarker of Gaucher disease. Am J Hematol. 2016 Nov;91(11):1082-1089

5. Patterson M: Niemann-Pick disease type C. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2000. Updated August 29, 2019. Accessed February 4, 2021. Available at www.ncbi.nlm.nih.gov/books/NBK1296/

## 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 is determined by LC-MS/MS is used to calculate the concentration of in the sample.(Unpublished Mayo method)

### PDF Report

No

### Specimen Retention Time

2 months

### Performing Laboratory Location

Rochester

## Fees & Codes

### Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test 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 | Reporting Name | LOINC® |
|---|---|---|
| 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 |