# Test Definition: HSMWB

Hepatosplenomegaly Panel, B

## Overview

### Useful For

As a component of the initial evaluation of a patient presenting with hepatosplenomegaly

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

### Genetics Test Information

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.

Although Fabry disease does not have hepatosplenomegaly as a clinical symptom, it can be identified by this assay as the compound, globotriaosylsphingosine, is detected.

### Method Name

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

### NY State Available

Yes

## Specimen

### Specimen Type

Whole blood

### Ordering Guidance

This test should not be used for monitoring patients with confirmed diagnoses. If a physician is requesting testing for monitoring purposes, see:

-CTXWB / Cerebrotendinous Xanthomatosis, Blood

-GPSYW / Glucopsychosine, Blood

-OXYWB / Oxysterols, Blood

This test's clinical sensitivity and specificity for the identification of Niemann-Pick type C (NPC) is 75% and 89%, respectively. If NPC is strongly suspected, HSMP / Hepatosplenomegaly Panel, Plasma is recommended.

### Specimen Required

**Container/Tube:**

**Preferred:** Lavender top (EDTA)

**Acceptable:** Green top (sodium heparin, lithium heparin), yellow top (ACD B)

**Specimen Volume:** 1 mL

## 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 |
|---|---|---|---|
| Whole blood | Refrigerated (preferred) | 72 hours | |
| | Ambient | 48 hours | |

# Clinical and 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 with a lower sensitivity and specificity C.

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

### Conditions Identifiable By Method

| Disorder | Onset | Analyte detected | Gene | Incidence |
|---|---|---|---|---|
| | | | | |

| | | | | |
|---|---|---|---|---|
| Cerebrotendinous xanthomatosis (CTX) | Infancy - adulthood | 7-Alpha-hydroxy-4-cholesten-3-one (7aC4)<br><br>7-alpha,12-aplha-dihydroxycholest-4-en-3-one (12aC4) | *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 2-4.Â  Patients with type 3 may have a less progressive phenotype and may survive into adulthood.Â | | | |
| 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 Fabry disease may also be identified by this assay. The glycosphingolipid, globotriaosylsphingosine (LGb3), may be elevated in symptomatic patients and supports a diagnosis of Fabry disease. Normal values of LGb3 do not rule out Fabry disease. Patients with Fabry disease do not have hepatosplenomegaly as an accompanying feature.

## Reference Values

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

Cutoff: < or =0.800 nmol/mL

LYSO-SPHINGOMYELIN

Cutoff: < or =0.100 nmol/mL

GLUCOPSYCHOSINE

Cutoff: < or =0.040 nmol/mL

7-ALPHA-HYDROXY-4-CHOLESTEN-3-ONE (7aC4)

Cutoff: < or =0.750 nmol/mL

7-ALPHA,12-ALPAH-DIHYDROXYCHOLEST-4-en-3-ONE (12aC4)

Cutoff: < or =0.250 nmol/mL

GLOBOTRIAOSYLSPHINGOSINE

Cutoff: < or =0.034 nmol/mL

## Interpretation

An elevation of 7-alpha-hydroxy-4-cholesten-3-one (7aC4) and 7-alpha,12-alpha-dihydroxycholest-4-en-3-one (12aC4) is strongly suggestive of cerebrotendinous xanthomatosis (CTX).

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).

An elevation of glucopsychosine is indicative of Gaucher disease.

### 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;55:146-154

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, 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;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

Whole blood is spotted on filter paper and dried overnight. A 3-mm dried blood spot is extracted with internal standard. The extract is subjected to liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. The MS/MS is operated in the multiple reaction monitoring (MRM) 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

### Day(s) Performed

Tuesday

### Report Available

2 to 9 days

### Specimen Retention Time

Whole blood: 7 days Dried Blood Spot: Normal results: 2 months; Abnormal result: Indefinitely

### Performing Laboratory Location

Rochester

## Fees and 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 Regional Manager. 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. 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 |
|---|---|---|
| HSMWB | Hepatosplenomegaly Panel, B | 92744-2 |

| Result ID | Test Result Name | Result LOINC Value |
|---|---|---|
| 601534 | Interpretation (HSMWB) | 59462-2 |
| 601528 | Cholestane-3beta,5alpha,6beta-triol | 92756-6 |
| 601529 | Lyso-sphingomyelin | 92748-3 |
| 601530 | Glucopsychosine | 92751-7 |
| 601531 | 7a-hydroxy-4-cholesten-3-one | 92762-4 |
| 601532 | 7a,12a-dihydroxycholest-4-en-3-one | 92759-0 |
| 601533 | Globotriaosylsphingosine | 92753-3 |
| 601535 | Reviewed By | 18771-6 |