MAYO CLINIC LABORATORIES

# Test Definition: PSYCF

Psychosine, CSF

## Overview

### Useful For

Aids in the biochemical diagnosis of Krabbe disease using cerebrospinal fluid specimens
Follow-up of individuals affected with Krabbe disease
Follow-up testing after an abnormal newborn screening result for Krabbe disease
Monitoring of individuals at risk to develop late onset Krabbe disease
Monitoring of individuals with Krabbe disease after hematopoietic stem cell transplantation

### Genetics Test Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal disorder caused by deficient activity of the enzyme galactocerebrosidase.
Krabbe disease is clinically variable and infantile-onset Krabbe disease is the most severe variant with rapid neurological regression resulting in early death.

### Highlights

This test is used as a biomarker of Krabbe disease for individuals with reduced galactocerebrosidase (GALC) activity.
For cerebrospinal fluid (CSF) testing, psychosine is typically ordered when CSF is collected primarily to determine protein content in a patient at risk of or monitored for the development of signs of Krabbe disease.
Elevations in psychosine support a diagnosis of Krabbe disease; therefore, psychosine quantitation is a useful biomarker in determining if an individual has active disease. In addition, psychosine may be a valuable biomarker to monitor disease progression or treatment response.
Psychosine may also be elevated in saposin A cofactor deficiency, which results in a similar clinical phenotype to Krabbe disease, but patients typically have normal GALC activity in vitro.

### Method Name

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

### NY State Available

Yes

## Specimen

### Specimen Type

CSF

### Shipping Instructions

Send on dry ice. Avoid freeze thaw cycles.

### Necessary Information

**1. Patient's age is required.**
2. Date of hematopoietic stem cell transplantation (HSCT), if performed.

### Specimen Required

**Collection Container/Tube:** Sterile vial.
**Specimen Volume:** 0.15 mL
**Collection Instructions: Do not aliquot**.

### Forms

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

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |

### Specimen Minimum Volume

0.1 mL

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| CSF | Frozen (preferred) | 7 days | |

## Clinical & Interpretive

### Clinical Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal disorder caused by deficient activity of the enzyme galactocerebrosidase (GALC). GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates, galactosylceramide, lactosylceramide, and lactosylsphingosine. Krabbe disease is caused by variants in the *GALC* gene, and it has an estimated frequency of 1 in 250,000 births.

Eighty-five percent to 90% of patients present before the first year of life with central nervous system impairment including increasing irritability, developmental delay, and sensitivity to stimuli. Rapid neurodegeneration including white matter disease follows, with death usually occurring by 2 years of age. Ten percent to 15% of individuals have later onset variants of the disease that are characterized by ataxia, vision loss, weakness, and psychomotor regression, presenting anytime from 6 months to the seventh decade of life. The clinical course of Krabbe disease can be variable, even within the same family.

Newborn screening for Krabbe disease has been implemented in some states. The early (presymptomatic) identification and subsequent testing of infants at risk for Krabbe disease may be helpful in reducing the morbidity and mortality associated with this disease. While treatment is mostly supportive, hematopoietic stem cell transplantation has shown some success if performed prior to onset of neurologic damage.

Psychosine is a neurotoxin at elevated concentrations. Importantly, it is 1 of 4 substrates degraded by GALC. It has been shown to be elevated in patients with active Krabbe disease or with saposin A cofactor deficiency and, therefore, may be a useful biomarker for the presence of disease or disease progression.

Reduced or absent GALC in leukocytes (CBGC / Galactocerebrosidase, Leukocytes) or dried blood spots (PLSD / Lysosomal and Peroxisomal Storage Disorders Screen, Blood Spot) along with psychosine analysis can indicate a diagnosis of Krabbe disease. Molecular sequencing of the *GALC* gene (KRABZ / Krabbe Disease, Full Gene Analysis and Large [30 kb] Deletion, Varies) allows for detection of the disease-causing variants in affected patients and carrier detection in family members.

Individuals with a disease phenotype similar to Krabbe disease may have saposin A cofactor deficiency. Saposin A cofactor deficiency also results in elevated psychosine levels. Testing for this condition via molecular analysis of *PSAP* is

useful in those with elevated psychosine and normal to reduced GALC activity with normal molecular genetic *GALC* sequencing.

### Reference Values
Normal < 0.04 nmol/L

### Interpretation
An elevation of psychosine is indicative of Krabbe disease or saposin A cofactor deficiency.

### Cautions
Asymptomatic patients with later onset Krabbe disease may have a normal psychosine concentration in cerebrospinal fluid.

### Clinical Reference
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2. Orsini JJ, Escolar ML, Wasserstein MP, et al: Krabbe Disease. In: Adam MP, Ardinger HH, Pagon R, eds. GeneReviews[Interntet]. University of Washington, Seattle; 2000. Updated October 11, 2018. Accessed December 7, 2021. Available at: www.ncbi.nlm.nih.gov/books/NBK1238/
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4. Wenger DA, Escolar ML, Luzi P, Rafi MA: Krabbe disease (globoid cell leukodystrophy). In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed November 16, 2021. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546481&bookid=2709
5. Guenzel AJ, Turgeon CT, Nickander KK, et al: The critical role of psychosine in screening, diagnosis, and monitoring of Krabbe disease. Genet Med. 2020 Jun;22(6):1108-1118
6. Thompson-Stone R, Ream MA, Gelb M, et al: Consensus recommendations for the classification and long-term follow up of infants who screen positive for Krabbe disease. Mol Genet Metab. 2021 Sep-Oct;134(1-2):53-59

## Performance

### Method Description
Psychosine is extracted from cerebrospinal fluid and quantified using an isotopically labeled internal standard by liquid chromatography-tandem mass spectrometry.(Unpublished Mayo method)

### PDF Report
No

### Specimen Retention Time
Indefinitely

### 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