

## Overview

### Useful For

Aiding in the biochemical diagnosis of Krabbe disease using whole blood 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

This test is used as a biomarker of Krabbe disease for individuals with reduced galactocerebrosidase (GALC) activity and for monitoring of patients with Krabbe disease and Saposin A cofactor deficiency.

### Highlights

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal disorder caused by deficient activity of the enzyme galactocerebrosidase (GALC).

Krabbe disease is clinically variable and infantile-onset Krabbe disease is the most severe variant with rapid neurological regression resulting in early death.

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

Whole blood

### Shipping Instructions

Must be sent refrigerated.

### Necessary Information

1. Patient's age is required.

2. Date of hematopoietic stem cell transplantation (HSCT), if performed.

## Specimen Required

### Collection Container/Tube:

**Preferred:** Lavender top (EDTA)

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

**Specimen Volume:** 2 mL

### Specimen Minimum Volume

0.5 mL

### Reject Due To

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated	7 days	

## Clinical and 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 mutations 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 (PSY) 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 (GALCW / 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, PCR, Varies) allows for detection of the disease-causing mutations 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 moderately reduced GALC activity with normal molecular genetic GALC analysis.

### Reference Values

Normal <10 pmol/g Hb

### 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 CSF.

### Clinical Reference

1. Kwon JM, Matern D, Kurtzberg J, et al: Consensus guidelines for newborn screening, diagnosis and treatment of infantile Krabbe disease. *Orphanet J Rare Dis.* 2018;13(1):30 doi: 10.1186/s13023-018-0766-x
2. Orsini JJ, Escolar ML, Wasserstein MP, et al: Krabbe Disease. In *GeneReviews* Edited by: MP Adam, HH Ardinger, RA Pagon: University of Washington, Seattle. 1993-2019. 2000 Jun 19 [Updated 2018 Oct 11]. Accessed May 2019. Available at: [www.ncbi.nlm.nih.gov/books/NBK1238/](http://www.ncbi.nlm.nih.gov/books/NBK1238/)
3. Turgeon CT, Orsini JJ, Sanders KA, et al: Measurement of psychosine in dried blood spots - a possible improvement to newborn screening programs for Krabbe disease. *J Inher Metab Dis.* 2015;38: 923-929
4. Wenger DA, Escolar ML, Luzi P, Rafi MA: Krabbe disease (Globoid Cell Leukodystrophy). In *The Online Metabolic and Molecular Bases of Inherited Disease*. Edited by D Valle, AL Beaudet, B Vogelstein, KW Kinzler, SE Antonarakis, A Ballabio, K Gibson, G Mitchell. New York, NY: McGraw-Hill; 2014 Accessed March 20, 2019. Available at: <http://ommbid.mhmedical.com/content.aspx?bookid=971&sectionid=62644214>

### Performance

#### Method Description

Psychosine is extracted from washed red blood cells and quantified using an isotopically labeled internal standard by LC-MS/MS. (Unpublished Mayo method)

#### PDF Report

No

#### Day(s) and Time(s) Test Performed

Tuesday, Thursday; 8 a.m.

#### Analytic Time

3 days

#### Maximum Laboratory Time

7 days

#### Specimen Retention Time

---

1 year

**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 U.S. Food and Drug Administration.

**CPT Code Information**

82542

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
PSYR	Psychosine, RBC	93687-2

Result ID	Test Result Name	Result LOINC Value
606152	Interpretation (PSYR)	59462-2
606145	Psychosine, RBC	93687-2
606151	Reviewed By	18771-6