MAYO CLINIC LABORATORIES

Test Definition: PSY

Psychosine, Blood Spot

Overview

Useful For

Aids in the biochemical detection of Krabbe disease and saposin A cofactor deficiency

Second-tier testing or follow up testing after an abnormal newborn screening result in an infant for Krabbe disease

This test is **not** capable of identifying carriers of Krabbe disease.

This test is **not intended for** long-term monitoring of individuals being treated for Krabbe disease or for older children or adult patients at risk to develop Krabbe disease.

Genetics Test Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal storage disorder caused by an enzyme deficiency of galactocerebrosidase.

Although Krabbe disease is clinically variable, the most common and severe form of the disorder is early infantile onset that presents with rapid neurological regression and results in early death.

This test is a second-tier assay for infants who have abnormal newborn screening results with reduced GALC activity and can detect patients with infantile or late infantile Krabbe disease or saposin A cofactor deficiency.

Testing Algorithm

If the patient has abnormal newborn screening result for Krabbe disease, immediate action should be taken. Refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1,2)

The following are available:
-Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase
-Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine

Special Instructions

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine
- Blood Spot Collection Instructions

Highlights

Elevations in psychosine support a diagnosis of Krabbe disease; therefore, psychosine quantitation is a useful biomarker in determining if an individual has active disease.

Psychosine may also be elevated in saposin A cofactor deficiency, which results in a similar clinical phenotype to Krabbe

disease, but patients have normal galactocerebrosidase activity.

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

NY State Available
Yes

Specimen

Specimen Type
Whole blood

Ordering Guidance
This test is recommended for newborns or infants who **have not had** previous psychosine testing. This test is **not intended** to be used as a monitoring test for individuals with Krabbe disease who are treated or for children or adults at risk of developing Krabbe disease. For patients older than infancy, order PSYR / Psychosine, Whole Blood.

Specimen Required
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Card-Blood Spot Collection (Filter Paper)
Acceptable: PerkinElmer 226 filter paper, Munktell filter paper, Whatman protein Saver 903 paper, local newborn screening card, or blood collected in tubes containing EDTA (preferred) or heparin and dried on filter paper
Specimen Volume: 2 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. Completely fill at least 2 circles on the filter paper card (approximately 100 microliters blood per circle).
3. Let blood dry on filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. Keep specimen dry.
Additional Information:
1. For collection instructions, see Blood Spot Collection Instructions
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

Forms
1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

1 Blood spot

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Nonapproved filter paper	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	96 days	FILTER PAPER
	Refrigerated	96 days	FILTER PAPER
	Frozen	96 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal storage disorder caused by an enzyme deficiency of galactocerebrosidase (GALC). GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates, galactosylceramide, lactosylceramide, and lactosylsphingosine. Krabbe disease is caused by disease-causing variants in the *GALC* gene.

Severely affected individuals typically present between 3 to 6 months of age with increasing irritability and sensitivity to stimuli. Rapid neurodegeneration, including white matter disease, follows with death usually occurring by 2 years old. Some individuals have later onset forms of the disease that are characterized by ataxia, vision loss, weakness, and psychomotor regression presenting anywhere from 1 year 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 early, prior to onset of neurologic damage.

Psychosine is 1 of 4 substrates degraded by GALC and is a neurotoxin at elevated concentrations. 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 elevated psychosine levels can indicate a diagnosis of Krabbe disease. Molecular sequencing of the *GALC* gene (GALC / Krabbe Disease, *GALC* Gene Sequencing with Deletion/Duplication, 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 the *PSAP* gene is useful in those with elevated psychosine and normal to reduced GALC activity with normal molecular genetic *GALC* sequencing.

Reference Values

Normal <2 nmol/L

Interpretation

An interpretive report will be provided.

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

When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing and in vitro confirmatory studies (enzyme assay, molecular analysis), and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Cautions

Normal psychosine levels may be seen in patients (from childhood to adulthood) who are not yet symptomatic or have later onset Krabbe disease or saposin A cofactor deficiency.

Supportive Data

Receiver operating characteristic curve analysis of 220 controls and 6 patients affected with Krabbe disease yielded an area under the curve of 1.0, permitting the selection of a cutoff value yielding a positive predictive value and negative predictive value of 1.0.

Clinical Reference

1. Newborn Screening ACT Sheet [Decreased galactocerebrosidase, elevated psychosine] Krabbe Disease (infantile form). American College of Medical Genetics and Genomics; 2021. Updated May 2022. Accessed October 2, 2025. Available at www.acmg.net/PDFLibrary/Krabbe-Infantile.pdf
2. Newborn Screening ACT Sheet [Decreased galactocerebrosidase, mildly elevated psychosine] Krabbe Disease (late-onset form). American College of Medical Genetics and Genomics; 2021. Updated May 2022. Accessed October 2, 2025. Available www.acmg.net/PDFLibrary/Krabbe-Later-Onset.pdf
3. 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 October 2, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546481&bookid=2709
4. Guenzel AJ, Turgeon CT, Nickander KK, et al. The critical role of psychosine in screening, diagnosis, and monitoring of Krabbe disease. Genet Med. 2020;22(6):1108-1118. doi:10.1038/s41436-020-0764-y

5. 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;134(1-2):53-59. doi:10.1016/j.ymgme.2021.03.016
6. Matern D, Basheeruddin K, Klug TL, et al. Newborn Screening for Krabbe Disease: Status Quo and Recommendations for Improvements. Int J Neonatal Screen. 2024;10(1):10. doi:10.3390/ijns10010010

Performance

Method Description
Internal standard is added to a dried blood spot. The extract is evaporated and reconstituted prior to injection onto a liquid chromatography tandem mass spectrometry (LC-MS/MS). Following separation of the structural isomers glucopsychosine and psychosine (PSY) by liquid chromatography, their concentrations are measured by MS/MS analysis in the multiple reaction monitoring positive mode to follow the precursor to product species transitions for PSY. The ratio of the extracted peak area of PSY to internal standard as determined by LC-MS/MS is used to calculate the concentration of PSY in the sample.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Sunday

Report Available
1 to 2 days

Specimen Retention Time
1 year

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
PSY	Psychosine, BS	93688-0

Result ID	Test Result Name	Result LOINC® Value
62235	Psychosine	93688-0
36342	Reviewed By	18771-6
36343	Interpretation (PSY)	59462-2