Overview

Useful For
Diagnosis of Krabbe disease
Follow-up testing for evaluation of an abnormal newborn screening result for Krabbe disease
This test is not intended for carrier detection.

Genetics Test Information
This test provides diagnostic testing for patients with clinical signs and symptoms suspicious for Krabbe disease.
Enzyme testing for galactocerebrosidase is included in the diagnostic workup for infants following a positive newborn screen result for Krabbe disease.

Testing Algorithm
The following are available in Special Instructions:

- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase, Psychosine, and GALC 30kb Deletion
- Newborn Screening Act Sheet Krabbe Disease: Decreased Galactocerebrosidase

Special Instructions
- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Newborn Screening Act Sheet Krabbe Disease: Decreased Galactocerebrosidase
- Informed Consent for Genetic Testing (Spanish)
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine
- Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase, Psychosine, and GALC 30kb Deletion

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

NY State Available
Yes

Specimen

Specimen Type
Whole Blood ACD

Advisory Information
This test will not detect carrier status. For differentiating alterations from disease-causing variants in affected patients
and for carrier detection in family members, molecular sequencing of the \textit{GALC} gene is necessary. Order KRABZ / Krabbe Disease, Full Gene Analysis and Large (30 kb) Deletion, PCR, Varies.

\textbf{Shipping Instructions}

For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerate within 96 hours of collection to be stabilized. Collect specimen Monday through Thursday only and not the day before a holiday. Specimen should be collected and packaged as close to shipping time as possible.

\textbf{Specimen Required}

\textbf{Container/Tube:}

\textbf{Preferred:} Yellow top (ACD solution B)

\textbf{Acceptable:} Yellow top (ACD solution A) or lavender top (EDTA)

\textbf{Specimen Volume:} 6 mL

\textbf{Collection Instructions:} Send specimen in original tube. Do not transfer blood to other containers.

\textbf{Forms}

1. \textit{New York Clients-Informed consent is required}. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
   - \textit{Informed Consent for Genetic Testing} (T576)
   - \textit{Informed Consent for Genetic Testing-Spanish} (T826)

2. \textit{Biochemical Genetics Patient Information} (T602) in Special Instructions

\textbf{Specimen Minimum Volume}

2 mL

\textbf{Reject Due To}

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\textbf{Specimen Stability Information}

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\textbf{Clinical and Interpretive}

\textbf{Clinical Information}

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive disorder caused by a deficiency of the enzyme, galactocerebrosidase (GALC). GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates (galactosylceramide, lactosylceramide and lactosylsphingosine...
causing severe demyelination throughout the brain. Krabbe disease is caused by variants in the \textit{GALC} gene, and it has an estimated frequency of 1 in 100,000 births. Although rare, a few infants with an early onset Krabbe disease phenotype due to deficiency of saposin A have been found. Saposin-A is a sphingolipid activator protein that assists galactocerebrosidase in its action on galactosylceramide.

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 age 2. Some individuals have later onset forms of the disease that are characterized by ataxia, vision loss, weakness, and psychomotor regression presenting anywhere from age 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.

Reduced or absent galactocerebrosidase in leukocytes can indicate a diagnosis of Krabbe disease, however a number of alterations in the \textit{GALC} gene have been identified that result in reduced galactocerebrosidase activity in vitro, but do not cause disease. The biomarker, psychosine (see PSY / Psychosine, Blood Spot) has been shown to be elevated in patients with active Krabbe disease. Molecular sequencing of the \textit{GALC} gene (see KRABZ / Krabbe Disease, Full Gene Analysis and Large [30 kb] Deletion, PCR, Varies) is necessary for differentiating alterations from disease-causing variants in affected patients and for carrier detection in family members.

**Reference Values**

\begin{align*}
> \text{or} =0.30 \text{ nmol/hour/mg protein}
\end{align*}

An interpretative report will be provided.

**Interpretation**

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), name and number of key contacts who may provide these studies, and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

**Cautions**

Pseudodeficiency of galactocerebrosidase causes reduced enzymatic activity but does not cause disease.

A Krabbe disease phenotype can also be caused in very rare cases by the absence of a physiologically active sphingolipid activator protein, saposin A.

Enzyme levels may be normal in individuals who have undergone hematopoietic stem cell transplant.

**Clinical Reference**


Test Definition: GALCW
Galactocerebrosidase, WBC


Performance

Method Description
The specimens are incubated with a mix of substrate and internal standard for galactocerebrosidase (GALC) and alpha-galactosidase (GLA). The reaction is then stopped using acetonitrile, centrifuged, and a portion of the supernatant is prepared for analysis by liquid chromatography-tandem mass spectrometry (LC-MS/MS). GLA is included to verify sample integrity. (Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Specimens are processed Monday through Sunday.

Assay is performed: Varies

Analytic Time
5 days

Maximum Laboratory Time
10 days

Specimen Retention Time
WBC homogenate; 1 month

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
82657

Document generated March 6, 2021 at 1:19pm CST
**Test Definition: GALCW**

Galactocerebrosidase, WBC

### LOINC® Information

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