ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

ACT Sheet

## Newborn Screening ACT Sheet

# [Decreased galactocerebrosidase, elevated psychosine]

## Krabbe Disease (infantile form)

**Differential Diagnosis:** Saposin A deficiency.

**Condition Description:** Krabbe disease (globoid cell leukodystrophy) is a lysosomal disorder caused by deficiency of galactocerebrosidase, resulting in impaired turnover of myelin with subsequent dysfunction and eventual loss of oligodendrocytes and Schwann cells. The infantile form usually presents before the first year of life. Newborns are asymptomatic and, if untreated, survival beyond age 2 years is uncommon.

***You Should Take the Following IMMEDIATE Actions:***

- Inform family of the newborn screening result.
- Ascertain clinical status (newborns are asymptomatic).
- Consult with or refer to pediatric metabolic and transplant specialist the same day.
- Evaluate the newborn (perform physical examination, newborns are expected to be asymptomatic).
- Initiate confirmatory/diagnostic testing, as recommended by the specialist.
- Provide the family with basic information about Krabbe disease and its management.

- Report final diagnostic outcome to newborn screening program.

**Diagnostic Evaluation:** Leukocyte galactocerebrosidase enzyme assay and measurement of erythrocyte psychosine concentration: Decreased enzyme activity is suggestive of Krabbe disease, but this result alone does not exclude pseudodeficiency, which causes decreased enzyme levels without disease. Combined evaluation of galactocerebrosidase activity and psychosine concentration predict the phenotype (unaffected vs. early vs. late onset Krabbe disease). Molecular genetic testing can confirm the diagnosis.

**Clinical Considerations:** The clinical presentation of Krabbe disease ranges from a rapidly progressive infantile form to more slowly progressive later-onset variants. All forms of Krabbe disease are associated with leukodystrophy, but the age of onset and rate of progression vary widely. The only available therapy is hematopoietic stem cell transplantation that is most effective if performed before 30 days of life in patients with the infantile form or prior to the onset of clinical symptoms in the late-onset forms. Gene therapy and other clinical trials may be available. Saposin A deficiency has been described in <10 patients, is clinically very similar to Krabbe disease, and may be detectable by newborn screening.

**Additional Information:**

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
Condition Information for Families- HRSA Newborn Screening Clearinghouse

**Referral (local, state, regional, and national):**

Find a Genetics Clinic Directory
Genetic Testing Registry

 *(Funded in part through MCHB/HRSA/HHS grant #U22MC03957;#UH9MC30770; National Coordinating Center for the Regional Genetics Networks)*

## Local Resources *(Insert Local Website Links)*

### State Resource Site (Insert Website Information)

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| **Name** | |
| **URL** | |
| **Comments** | |

### Local Resource Site (Insert Website Information)

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| **Name** | |
| **URL** | |
| **Comments** | |

## Appendix *(Resources with Full URL Addresses)*

### Additional Information

How to Communicate Newborn Screening Results
- https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/Resources/achdnc-communication-guide-newborn.pdf

Gene Reviews
- https://www.ncbi.nlm.nih.gov/books/NBK1238/

Medline Plus
- https://medlineplus.gov/genetics/condition/krabbe-disease/

Condition Information for Families-HRSA Newborn Screening Clearinghouse
- https://newbornscreening.hrsa.gov/conditions/krabbe-disease

### Referral (local, state, regional and national)

Find a Genetics Clinic Directory
- https://clinics.acmg.net

Genetic Testing Registry
- https://www.ncbi.nlm.nih.gov/gtr/