WISCONSIN NEWBORN SCREENING (NBS) PROGRAM – CONDITION NOMINATION

Nomination of a Condition to the Wisconsin Newborn Screening Panel

Date of Nomination

3/17/2025

NOMINATOR	
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CO-SPONSORING ORGANIZATION #1 (as appropriate, additional sponsors may be included on page 5)	
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Condition	**STATEMENT**
Nominated Condition	Krabbe disease -Consideration for Infantile Krabbe disease only (psychosine at or above 10 nmol/L) vs. all Krabbe disease (psychosine at or above 2 nmol/L).
Description of Disorder	Krabbe disease is an inherited progressive neurological disorder that results in leukodystrophy which results in early death [1]. This genetic condition follows an autosomal recessive inheritance pattern, in which biallelic pathogenic variants in the GALC gene result in a deficiency of the enzyme galactocerebrosidase (GALC) [2]. GALC is an enzyme that normally breaks down psychosine and other sphingolipids, and the absence of GALC leads to the toxic buildup of psychosine [3]. The buildup of psychosine disrupts normal cellular functions and induces cell death in oligodendrocytes and Schwann cells, the cells responsible for producing myelin in the CNS and PNS respectively. Myelin forms protective sheaths around nerve fibers, enabling efficient transmission of nerve signals. When myelin breaks down- a process called demyelination- the central nervous system is severely affected, resulting in neurodegeneration and early death.
Screening Method	-1st tier measurement of GALC enzyme activity using MS/MS on dried blood spot (DBS) -2nd tier measurement of psychosine level on residual DBS
Gene	GALC

OMIM or other names for condition	-OMIM ID: 245200 -Globoid cell leukodystrophy -Globoid cell leukoencephalopathy -Galactosylceramide beta-galactosidase deficiency -Galactocerebrosidase deficiency -GALC deficiency
Case Definition	Krabbe disease- defect in GALC enzyme due to autosomal recessive inheritance of biallelic pathogenic variants in the GALC gene causing accumulation of psychosine and resulting in neurodegeneration and early death. -Infantile Krabbe Disease: Reduced or absent GALC enzyme and psychosine 10 or greater nmol/L -Late-onset Krabbe Disease + Infantile Krabbe Disease: Reduced GALC and Psychosine 2 or greater

NOTE: Please reference each statement/answer with the corresponding reference number listed in **Key References**.

CRITERION

Criterion 1: Mandated testing should be limited to conditions that cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening.	
Timing of Clinical Onset	*Relevance of the timing of newborn screening to onset of clinical manifestations. Must cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening.* In the early infantile form of Krabbe disease, infants appear healthy at birth but typically have a median onset of severe neurological symptoms around 4 to 6 months of age. Around 62% of Krabbe cases present as the early infantile form [4]. Early symptoms include irritability, twitching, hypotonia, episodic fevers, feeding difficulties, vomiting, hypersensitivity to external stimuli, seizures, and delays in both mental and motor development [5]. As the disease progresses, infants experience muscle weakness, spasticity, deafness, and blindness [6]. Affected infants typically die within the first two years of life without early treatment [7]. Hematopoietic stem cell treatment (HSCT) is currently the most effective treatment for slowing the progression of Krabbe disease. For HSCT to have the best outcomes in those with infantile Krabbe disease, it must be performed within the first 30 days of life, and ideally no later than 45 days[8]. Early detection is crucial, either through a family history or newborn screening, to identify infants before they develop symptoms [1]. Once symptoms appear, irreversible neurological damage has already occurred, making HSCT less effective and resulting in significant morbidity, mortality, and low survival rate [9,10]. Without a family history, NBS offers the only chance of identifying these patients before symptoms occur. The federal advisory committee voted to recommend the addition of Infantile Krabbe disease with psychosine 10 or greater to their Recommended Newborn Screening Panel (RUSP) on January 30, 2024. On July 1, 2024 the U.S. Secretary of Health officially added Krabbe to the RUSP. Since this addition to the RUSP, three states—Kansas, Michigan, and Iowa—have been in discussions to add Krabbe. Seven states—Texas, North Carolina, Maryland, Connecticut, California, Utah, and Oregon—have officially begun the process of implementing KD in NBS. In addition, Florida, Arizona, Alabama, Oklahoma, Arkansas, and Mississippi have RUSP alignment laws and will begin screening in the next few years. As of now, Oregon has decided to implement NBS for early infantile KD only and use a PSY cutoff of 10 or greater for second tier testing. All other states are deciding whether to follow the RUSP recommendation or to follow what the other 10 states using PSY have done, which is a cutoff of 1.5-2. The other form of Krabbe disease is late-onset Krabbe. Around 37% of those with Krabbe disease have a late-onset form [11]. The late onset form can be further broken up into 3 categories: •Late infantile: 1 year to less than or equal to 4 years •Juvenile: 4 years to less than or equal to 18 years •Adult: 18 years or greater Late infantile Krabbe disease patients experience a slower progression and variable symptoms which may include vision loss, psychomotor regression, spastic paraparesis, and gait abnormalities [12]. The juvenile and adult forms typically present as gait abnormalities, ataxia, spastic paraparesis, and vison and hearing loss [12,13]
Criterion 2: For each condition, there should be information about the incidence, morbidity and mortality, and the natural history of the disorder.	

Incidence	*Determined by what method(s): pilot screening or clinical identification?* -1 in 100,000-250,000 in the US (Genereviews)[5] -Illinois: 1 in 250,000 [14] -New York: 1 in 394,000 [11] -Determined by clinical identification in each state -Early-Infantile Krabbe: 62% of cases [4] -Late-Infantile: 10% of cases [4] -Juvenile: 22% of cases [4] -Adult: 5% of cases [4]
Severity of Disease	*Morbidity, disability, mortality, spectrum of severity, natural history*. In the infantile form, infants appear healthy at birth but typically have a median onset of symptoms around 6 months of age. Early symptoms include irritability, twitching, spasticity, hypotonia, episodic fevers, feeding difficulties, vision loss, hearing issues, vomiting, hypersensitivity to external stimuli, seizures, and delays in both mental and motor development [5]. As the disease progresses, infants experience muscle weakness, spasticity, deafness, and blindness [6]. Without treatment, affected infants typically pass away within two years of life [7,12]. Death from Krabbe disease usually results from respiratory failure due to poor muscle tone or infections from aspiration. Late infantile Krabbe disease patients experience a slower progression and variable symptoms which may include vision loss, psychomotor regression, spastic paraparesis, and gait abnormalities [12]. The juvenile and adult forms typically present as gait abnormalities, ataxia, spastic paraparesis, and vison and hearing loss [12,13]. The late-infantile die within two years of birth, juvenile die within 10 years of birth. The progression of disease and lifespan reduction varies in adult-onset Krabbe disease [15].

Criterion 3: Conditions identified by newborn screening should be linked with interventions that have been shown in well-designed studies to be safe and effective in preventing serious health consequences.	
Urgency	How soon after birth must treatment be initiated to be effective? Hematopoietic stem cell treatment (HSCT) is currently the most effective treatment for slowing the progression of Krabbe disease [16]. Early detection is crucial, either through a family history or newborn screening, to identify infants before they develop symptoms [17]. Treatment must occur before the presence of severe, irreversible signs and symptoms [8]. For HSCT to have the best outcomes, it must be performed within the first 30 days of life and no later than 45 days, as infants who undergo HSCT before 30 days experience improved survival and better outcomes in communication, feeding, and mobility compared to those transplanted after 30 days[8,17]. Psychosine, the substrate that causes the neurological decline, has been shown to decrease in patients after transplantation, supporting this treatment at a biological level [18]. Individuals who undergo transplantation after the onset of symptoms have poor functional outcomes and a lower likelihood of survival [19] . Without a family history, NBS offers the only chance of identifying these patients before symptoms occur.

Efficacy (Benefits)	Extent of prevention of mortality, morbidity, disability. Treatment limitations, such as difficulty with acceptance or adherence. Early hematopoietic stem cell transplantation (HSCT) in presymptomatic infants with infantile Krabbe disease has been shown to significantly improve both survival and neurological outcomes. When HSCT is performed urgently, ideally before 30 days of age, it provides significant survival and functional benefits in presymptomatic infants with infantile Krabbe disease [20] . Specifically, asymptomatic patients who received HSCT had a median survival of 15.5 years, compared to just 2.2 years in the untreated group. Furthermore, infants who underwent HSCT after symptom onset had a median survival of only 5 years [12][21]. In terms of functional outcomes, asymptomatic infants who received HSCT showed superior cognitive, motor, and adaptive development, better vision and hearing, and fewer feeding difficulties compared to symptomatic patients who received HSCT or untreated individuals [12][21]. Treatment with HSCT has allowed some children to lead relatively normal lives up to their early teen years, demonstrating that the age at transplantation plays a key role in long-term outcomes [22]. While HSCT does not cure Krabbe disease, it stops or significantly delays disease progression, extending both survival and quality of life. However, families should be informed that the treatment does not completely prevent long-term motor and speech difficulties, and children may require ongoing special services [22]. Further evidence underscores the critical importance of early intervention. Infants transplanted at less than 30 days of age exhibit more favorable outcomes in communication, feeding, and mobility compared to those transplanted after 30 days but before 61 days of life. Therefore, early diagnosis and swift decision-making regarding HSCT are essential to optimizing long-term functional outcomes for presymptomatic newborns diagnosed with Krabbe disease [17]. In contrast, untreated infants typically develop severe motor delays, quadriparesis, autonomic instability by one year, and early death, highlighting the benefits of early HSCT. While developmental delays are often associated with HSCT itself, these delays are far less severe than the neurological impairments seen in untreated infants [20]. A study was done of a postmortem examination of an untreated Krabbe disease patient compared to a patient with infantile Krabbe disease who underwent HSCT in infancy. The patient who received a transplantation showed remarkable improvement in brain pathology. Imaging and histological analysis revealed no evidence of globoid cells (which are indicative of Krabbe disease) or active demyelination in the central nervous system (CNS). This suggests that the HSCT led to partial restoration of the CNS, as the transplanted cells likely differentiated into microglial cells and oligodendrocytes, promoting a reduction in the toxic accumulation of psychosine and halting the demyelination process [23].

Potential Harms	Potential medical or other ill effects from treatment. Mortality- Up to 10% mortality in early HSCT (Dr. Kurtzberg personal communication) Hematopoietic stem cell transplantation (HSCT) provides significant survival and functional benefits for infants with early-infantile Krabbe disease, but the procedure does carry notable risks. The transplantation requires patients to undergo chemotherapy or radiation to destroy their own cells, allowing donor cells to take their place [17]. This myeloablative treatment can lead to serious side effects, including immunosuppression, increased vulnerability to infections, and damage to vital organs such as the liver and kidneys[21]. Additionally, there is a risk of developing graft-versus-host disease (GVHD), where the transplanted donor cells attack the recipient's tissues, which can further complicate recovery and impact quality of life[17]. Post-transplant, children can experience challenges, including global developmental delays, peripheral neuropathy symptoms, and cognitive disabilities. Although the procedure has been shown to stabilize disease in presymptomatic infants, those who undergo HSCT after the onset of symptoms face poorer outcomes, with a higher risk of death and minimal neurological improvements from the transplant [21]. A study was done of a postmortem examination of an untreated Krabbe disease patient compared to a patient with infantile Krabbe disease who underwent HSCT in infancy. As stated earlier, the individual did show improvement in the central nervous system (CNS) but, the treatment was less effective in the peripheral nervous system (PNS). Many transplanted patients still experience limited clinical improvement in the PNS, with only transient improvements in nerve conduction velocities and persistent nerve pathology, including myelin loss and axonal damage. This disparity in effectiveness between the CNS and PNS may be due to the limited ability of HSCT to correct the metabolic defect in Schwann cells, which are essential for PNS myelination [23].
Criterion 4: The interventions should be reasonably available to affected newborns.	

Modality	*Drug(s), diet, replacement therapy, transplant, surgery, other. Include information regarding regulatory status of treatment.* The current standard of care for KD is hematopoietic stem cell transplantation (HSCT). HSCT introduces donor-derived cells, which offer cross correction to GALC deficient oligodendrocytes in the brain [12]. HSCT involves harvesting healthy, enzyme producing stem cells from a compatible donor. Cells are obtained from umbilical cord blood, which is readily available for urgent transplants . An international cord blood registry (NMDP) allows for rapid identification of potential cord blood donor matches for transplant. It is also ethically acceptable for families of infants with early infantile Krabbe disease to choose not to pursue HSCT. This critical conversation should occur as soon as possible with the genetics, neurology and transplant team, with all benefits and risks outlined so that parents can make an informed choice.. Forge Biologics was conducting a gene therapy trial for Krabbe disease. The trial was recently discontinued due to financial reasons, but the community is working to determine a path forward to complete this phase of the trial. Furthermore, other companies are already interested in continuing trials, highlighting that gene therapy for Krabbe will continue to grow and develop. The REKLAIM trial evaluated FBX-101, an AAV-based intravenous gene therapy, administered after HSCT to treat infantile Krabbe. This approach leveraged the immune environment after HSCT to prevent immune responses to the gene therapy. FBX-101 provided GALC enzyme, potentially halting the neurodegenerative process. Results from five patients showed that FBX-101 was well tolerated, with no serious adverse events. In two myeloablated subjects, there were no immune responses to the treatment, and both demonstrated significant increases in GALC levels and a reduction in toxic psychosine levels. All five subjects also showed improved motor skills and normal brain development, suggesting that FBX-101 enhanced brain myelination and motor function. This treatment significantly improved outcomes for infantile Krabbe patients by offering better motor development and potential long-term benefits, with the possibility of redosing in the future [24].
Availability	*Describe scope of availability and note any limitations.* Infants born in WI have the option to receive HSCT at Children's WI, a premier transplant site in the state, or go to transplant centers in adjacent states, Lurie Children's in Chicago, IL, or University of Minnesota Fairview, MN. All offer high quality pediatric stem cell transplant options with experts. Per Dr. Alejandro Escobar-Vasco, MD, transplant fellow who trained with Dr. Kurtzberg at Duke and Dr. Julie-An Talno, Medical Director of the BMT center, Children's Wisconsin has a FACT accredited bone marrow transplant center with expertise in transplant for both malignant and non-malignant diseases including metabolic disease. They have the infrastructure and clinical experience to perform cord blood transplant in children of all ages including infants, and this can be performed on a urgent basis for Krabbe disease (personal communication, verbatim). Per Dr. Alejandro Escobar-Vasco, who has participated in the workgroup meetings to prepare for HSCT since their initiation, their team has consistently said that they can and are ready to do HSCT for KD. Dr. Escobar-Vasco is also a co-nominator who has contributed to the preparation of this nomination to add Krabbe disease to the WI NBS panel. WI Medicaid may pay for HSCT at these sites in IL or MN. Per Dr. Sonali Chaudhury, MD, Section Head- Stem Cell Transplantation and Cellular therapy Program at Lurie Children's Hospital in Chicago, IL, "our insurance team reviewed, and we have not had any patient from WI Medicaid receive a stem cell transplant at our center from 2009 onwards, but other organ transplants have been covered." Per the billing supervisor at U of MN-Fairview Pediatric Blood and Marrow Transplantation & Cellular Therapy program Allison Thao, "We have successfully obtained WI Medicaid coverage for many genetics patients from WI for HSCT at our center".

Criterion 5: Appropriate follow-up should be available for newborns that have a false positive newborn screen.	
Follow-up for False Positives	*Define the follow-up process.* Infants with normal GALC enzyme and normal psychosine and normal GALC molecular testing obtained at first clinic visit as confirmatory testing would be considered false positive NBS cases. These families would receive genetic counseling from expert metabolic centers to understand these results and lack of risk for disease. Infants with normal or reduced GALC enzyme, elevated psychosine, and normal GALC molecular testing should be offered additional sequencing of PSAP gene for possible Saposin A deficiency.
Criterion 6: The characteristics of mandated tests in the newborn population should be known, including specificity, sensitivity, and predictive value.	
Screening test(s) to be used	*Description of the high volume method, instrumentation and if available as part of multi-analyte platform.* The test is an FDA-approved 6 enzyme multiplex assay. The assay involves incubating a 3.2-mm dried blood spot punch with substrate and internal standard for GALC at 37°C for 18 hours. The products are purified, dried, suspended, and then analyzed using flow injection tandem mass spectrometry. The enzyme activities are calculated as the function of product per hour compared to the internal standard for the sample analysis. The current Krabbe screening assay is in a multiplex format. Besides GALC activity for Krabbe, the assay also includes ASM for Niemann–Pick disease, GLA for Fabry disease, IDUA for MPS I, ABG for Gaucher disease, and GAA for Pompe disease. When GALC activity is less than the cutoff value, the lab will review the other five enzyme activities. With one or more additional enzyme activity lower than 15% of the daily median, the specimen will be deemed as unsatisfactory. The multiplexing assay was chosen for specimen quality assessment, and to thereby reduce false positive results. Therefore, except for the targeted GALC, and GAA (currently used for Pompe disease screening) the other four enzyme activities are not reportable regardless of their values and no cutoffs have been developed.
Modality of Screening	*Dried blood spot, physical or physiologic assessment, other* Dried blood spot
Does the screening algorithm include a second tier test? If so, what type of test and availability?	*Dried blood spot, physical or physiologic assessment, other* Yes, specimens with low GALC enzyme lower than 15% of the daily median will then undergo 2nd tier testing measuring psychosine level. Infants with psychosine 10 nmol/L and greater would be considered at significant risk for infantile Krabbe disease. Individuals with intermediate elevation of psychosine 2-10 nmol/L would be considered at risk to develop later onset Krabbe disease.
Clinical Validation	*Location, duration, size, preliminary results of past/ongoing pilot study for clinical validation, positive predictive value, false positive rate, analytical specificity, sensitivity.* Programs that rely on PSY concentrations as a second-tier test have yielded the lowest false positive rates and the fastest referrals for identified infantile patients. Please see Tables 1 and 2 in the supplemental materials for comparison of PPV and false positive rates in states currently performing NBS for KD.
Analytic Validation	*Limit of detection/quantitation, detection rate, reportable range of test results, reference range. Include regulatory status of test, information about reference samples and controls required for testing and availability of or potential for external quality assurance system, e.g., QC and PT for both screening and confirmatory tests.* At this time, the verification study for GALC has not been done. An assay verification study will be done by WSLH newborn screening lab based on the CAP requirement before the screening implementation.

Potential Secondary Findings	*May other disorders be identified by the screening test for the nominated condition?* ☒ Yes ☐ No ***If yes:*** • *How should that identification be handled—should those screening results be disclosed to the physicians or parents?* Yes, pathogenic variants in the PSAP gene may lead to reduced GALC and elevated psychosine, a condition called Saposin A (PSAP) deficiency and may be detected by NBS. These results would mimic those of Krabbe disease, and so clinicians should be warned that infants with confirmatory clinical laboratory testing that shows reduced GALC, elevated or normal psychosine with normal GALC molecular testing, should then have molecular testing of PSAP to rule out Saposin A deficiency [25]. • *Would that disorder(s) meet the outlined criteria?* ☐ Yes ☒ No ○ *If yes, please prepare a separate nomination form for the secondary disorder(s)* ○ *If no, what criteria does it not meet?* This disorder would not meet outlined criteria in that it is rare and there is no treatment for Sap A deficiency [25].

Summary of Population-based Pilot Study(ies)

Location of Prospective Pilot	-Illinois [14] -New York [26]
Number of Newborns Screened	-IL: 494,147 between 12/8/2017- 12/31/2020 -NY: 2,090,910 specimens from 1,968,568 newborns between 2006-2014
Number of Positive Results	*Positive by primary test versus 2nd tier test if applicable.* -IL: 288 initially tested positive (13% batch median GALC activity) -NY: 10,199 initially tested positive (20% daily mean activity) -NY: After retest of GALC activity 620 samples had average activity of less than or equal to 12% and were reflexed to molecular analysis. -NY: Screen-positive results were obtained for 348 (0.17 per 1,000) infants who were referred to a Specialty Care Center for diagnostic workup.
False Positive Rate; False Negative Rate (if known)	*False positive by primary test versus 2nd tier test if applicable.* -NY: When analyzing molecular GALC, the referral rate was reduced ~43.8%
Number of Infants Confirmed with Diagnosis	*How are diagnosis confirmed [clinical, biochemical, molecular]?* -IL: 2 infantile. PSY (10-35nM) -IL: 6 late-onset, intermediate PSY levels (2-8.7nM) -IL: In this study molecular testing was also used as confirmation -NY: 5 confirmed infantile Krabbe -NY: 9 confirmed to be high-risk, presumed to be late-onset -As of 2023, 11 states were screening for KD, 9 of which used PSY as a second-tier test with a cutoff of 1.5-2. From 3.55 million infants screened by the 9 programs that use PSY, only 1,505 had a positive first tier test, and then 11 had a PSY of 10 or greater that was confirmed with follow up testing. One of these infants was lost to follow-up. Of the 10 remaining, 3 declined transplant, and 7 received transplant. One infant died of graft vs. host disease, and 6 were successfully transplanted and surviving with improved development (range 4-7 years) [27].
Criterion 7: If a new sample collection system is needed to add a disorder, reliability and timeliness of sample collection must be demonstrated.	
Is this a new sample collection system?	*If yes, demonstrate reliability and timeliness of sample collection process, including data collection, analysis, and reporting of new results.* No new sample collection required
Criterion 8: Before a test is added to the panel, the details of reporting, follow-up, and management must be completely delineated, including development of standard instructions, identification of consultants, and identification of appropriate referral centers throughout the state/region.	

Considerations of Screening and Diagnostic Testing	*False positives, carrier detection, invasiveness of method, other* False positives are minimal when PSY is used as a second tier test. PSY at 2 and greater will detect a few cases of infants who are heterozygous for one path GALC variant and/or multiple pseudodeficiency/polymorphic alleles, which can reduce the GALC enzyme to a degree that may overlap with later onset Krabbe disease. See supplemental tables 1 and 2. The method is no more invasive than the dried blood spots obtained for other NBS testing and the blood needed for confirmatory testing. .
Is test FDA cleared/approved	*Include availability of information, sole source manufacturer, etc.* Yes
List all CLIA or CAP certified labs offering testing in the US	*Link to GeneTests, and Genetic Test Reference if applicable.* PSY (newborn screening and clinical confirmatory testing): •Mayo Clinic Laboratories – PSY - https://www.mayocliniclabs.com/test-catalog/overview/62235 •Revvity – B0028 - https://www.revvity.com/test/Psychosine-Biochemical-Assay-B0028 •Greenwood Genetic Center - https://ggc.org/test-finder-item/krabbe-disease-psychosine-monitoring GALC (clinical confirmatory testing): •Thomas Jefferson Lab – https://www.jefferson.edu/academics/colleges-schools-institutes/skmc/departments/neurology/programs/neurogenetics/lysosomal-diseases/tests.html •Mayo Clinic Lab – GALCW - https://www.mayocliniclabs.com/test-catalog/overview/606270 •Greenwood Genetics Lab - https://ggc.org/test-finder-item/krabbe-disease-galactocerebrosidase-enzyme-analysis-dbs
Follow-up and management process	*Development of standard instructions, identification of consultants, identification of appropriate referral centers throughout the state/region, follow-up for results, management of ongoing care, education, and outreach.* Infants with low GALC and psychosine 10 or greater would be referred immediately for a clinic visit with a genetics and/or neurology expert at a center that can offer HSCT. Direct inpatient admission while working through counseling and confirmatory laboratory testing has proven the most efficient method to provide HSCT in the optimal timeframe for good clinical outcomes, should the parents choose to pursue it. Infants with low GALC and psychosine 2-9 are considered later-onset and should be seen in clinic and have confirmatory laboratory testing performed within days to a week. Infants with low GALC and normal psychosine would be reported as a normal NBS result and not referred for follow up, preventing a majority of false positive cases experienced in other states that provide NBS for KD that do not use a second tier test (OH and NJ). -HSCT centers – Childrens WI in Milwaukee, or optional referral to Dr. Jennifer Rubin at Lurie Children's in Chicago or Dr. Paul Orchard at U of MN Fairview in MN.
Criterion 9: Recommendations and decisions should include consideration of the costs of the screening test, confirmatory testing, accompanying treatment, counseling, and the consequences of false positives. The mechanism of funding those costs should be identified. Expertise in economic factors should be available to those responsible for recommendations and decisions.	
Screening test	-GALC enzyme from DBS as the first-tier testing -Psychosine level on DBS as the second-tier testing
Confirmatory testing	GALC enzyme in leukocytes, psychosine in erythrocytes/RBCs, and GALC molecular analysis are the recommended confirmatory tests to be performed as clinical follow up for an infant with a positive NBS.
Treatment	HSCT is the standard of care treatment for Krabbe disease, and ideally needs to be performed within the first 30 days of life and no later than 45 days

Counseling	Genetic counseling can be performed at any of the 2-3 regional medical centers in WI (Children's Wisconsin Genetics Center, Waisman Center Genetics Clinic – Madison, Marshfield Clinic Genetics Center).
False positives	Programs that rely on PSY concentrations as a second-tier test have yielded the lowest false positive rates and the fastest referrals for identified infantile patients.
Mechanism of funding	Wisconsin currently utilizes a 6 enzyme multiplex panel for Pompe disease NBS that includes the GALC enzyme that could be utilized for 1st tier Krabbe disease NBS at no additional cost. Second tier testing utilizing psychosine would be an additional cost. If the NBS lab uses an enzyme cutoff of 10% of the daily median, then we would expect 50 samples a year to be sent for second tier psychosine testing. If they use 15% of the daily median, then 150 samples would be anticipated to be sent out for second tier testing for psychosine ($60-100). Anticipated cost for clinical follow-up support; clinical FTE support has been provided to some genetics centers for clinical evaluation following abnormal NBS result.

Key References to support each criterion. Please list and attach as PDF(s). If mailing, include hard copies.	
#	**Criterion 1**
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	Criterion 7
	Criterion 8
	Criterion 9

Additional Co-sponsoring Organizations

CO-SPONSORING ORGANIZATION #2	
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CO-SPONSORING ORGANIZATION #5	
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Submission Checklist	
☒	Nomination form
☒	Conflict of Interest Forms completed by Nominator and all Co-Sponsoring Organizations
☒	PDF(s) or hard copies of references

Contact information of Nominator: Zoe Culshaw-Klein, zculshaw@mcw.edu

Submit Nominations to: DHSWICongenitalDisorders@wisconsin.gov
Or mail to:

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