Advisory Committee on Heritable Disorders in Newborns and Children

Advisory Committee on Heritable Disorders in Newborns and Children
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March 01, 2024

The Honorable Xavier Becerra
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Secretary Becerra:

This letter is to inform you of a new recommendation from the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC or Committee). As you are aware, the ACHDNC provides advice and recommendations concerning heritable disorders and newborn and childhood screening practices for these disorders. The objective of the ACHDNC is to enhance states' abilities to reduce morbidity and mortality in newborns and children who have, or who are at risk for, heritable disorders. The ACHDNC makes systematic evidence-based recommendations regarding conditions for inclusion on the Recommended Uniform Screening Panel (RUSP): the list of conditions you recommend states to screen as part of their state universal newborn screening programs. Newborn screening is a state public health function and most states screen for the majority of disorders on the RUSP.

On behalf of the ACHDNC, I would like to recommend that infantile Krabbe disease, as defined by low GALC enzyme activity and psychosine ≥10 nM, be added to the RUSP. This recommendation is based upon Committee deliberations and findings from two evidence reviews by the Committee (see attached reports) that describe the clinical data, testing methodology, available treatments, potential benefits and harms, an assessment of impact on the public health systems, and public comments.

Infantile Krabbe disease is a rare, heritable disorder that causes low levels of the galactocerebrosidase (GALC) enzyme. Low levels of the GALC enzyme result in the elevation of the toxic lipid, psychosine that causes the death of nerve cells, including those in the brain. When untreated, low levels of GALC and high levels of psychosine lead to feeding problems, significant irritability, difficulty moving, and progressive neurologic impairment by 12 months after birth with death in early childhood. Infantile Krabbe disease presents signs and symptoms within 12 months after birth. The prevalence of infantile

Krabbe disease based on newborn screening data from nine states is 0.31 per 100,000 (3.1 per 1 million) live births.

In February 2023, the ACHDNC voted to not recommend Krabbe disease (early and late infantile phenotypes) for inclusion on the RUSP. The Committee concluded that there was not sufficient evidence of significant net benefit to recommend population based newborn screening for Krabbe disease. In July 2023, the ACHDNC received a revised nomination for the detection of infantile Krabbe disease (low GALC enzyme activity and psychosine ≥ 10 nM). In August 2023, the Committee voted to conduct an expedited review of infantile Krabbe disease focusing on disease development in the first year of life. Based on new evidence and the narrower definition, in January 2024, the Committee voted to recommend the addition of infantile Krabbe disease to the RUSP.

Treatment for infantile Krabbe disease is hematopoietic stem cell transplant (HSCT) prior to the development of significant signs or symptoms of Krabbe disease. HSCT is recommended by 4 to 6 weeks after birth, before the development of significant disease. Based on available studies, treatment improves survival and developmental outcomes, such as communication and social interactions. HSCT extends life for infantile Krabbe disease, but the impact on neurologic outcomes and other outcomes are variable. There is the potential of mortality related to HSCT, and some families opt not to treat their affected child.

The Committee felt strongly that screening for infantile Krabbe disease should only be done using a two-tiered blood spot screening algorithm (first-tier low GALC enzyme activity and second-tier psychosine ≥10 nM). Currently, nine states are using the two-tiered blood spot screening algorithm successfully. The Committee noted that, according to a survey assessment, that most state laboratories will be able to implement screening in 2-3 years, with some taking more time due to local factors such as required policy changes, funding, and coordination of follow up treatment, and interaction with other state priorities. The process of diagnosing and treating infantile Krabbe disease within 4 to 6 weeks may be challenging, with potential for errors and delays. There are also potential equity concerns regarding the availability of appropriate donors for HSCT treatment of infants from under-represented minority populations.

The Committee deliberated on the net benefits of early screening and diagnosis, certainty of available evidence and feasibility of states screening for infantile Krabbe disease and determined that there is moderate certainty of significant benefits to infants identified with infantile Krabbe disease through newborn screening. There is a reliable screening, testing and treatment in state newborn screening systems. Georgia, Illinois, Indiana, Kentucky, Missouri, New York, Pennsylvania, South Carolina, and Tennessee have incorporated two-tier screening (first-tier screening for low GALC enzyme activity; second-tier psychosine testing) for infantile Krabbe disease into their newborn screening programs. The Centers for Disease Control and Prevention has developed quality assurance/quality control and proficiency testing materials for newborn screening laboratories to aid in the implementation of testing Krabbe disease.

After considering the available evidence, the Committee concluded that screening for infantile Krabbe disease (low GALC and psychosine ≥ 10) will lead to significant

benefits for infants born with this rare condition, we respectfully request you accept the recommendation to add infantile Krabbe disease (low GALC and psychosine ≥ 10) to the RUSP. As expressed during several Committee public comment periods, advocates and family organizations are interested in the outcome of this recommendation and are expecting a response within 120 days per the Newborn Screening Saves Lives Reauthorization Act of 2014.

Sincerely,

/s/

Ned Calonge, MD, MPH
Chairperson

Enclosures:
Reports – *Expedited Evidence-based Review of Newborn Screening for Krabbe Disease and Evidence-based Review of Newborn Screening for Krabbe Disease*

cc: CDR Leticia Manning, MPH
Designated Federal Official
Health Resources and Services Administration