



Advisory Committee on Heritable Disorders in Newborns and Children

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Newborns and Children
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www.hrsa.gov/advisory-committees/heritable-disorders

March 22, 2023

Hunter's Hope Foundation
P.O. Box 643
Orchard Park, NY 14127

Dear Hunter's Hope Foundation:

The Advisory Committee on Heritable Disorders in Newborns and Children (Committee) appreciates your nomination of Krabbe disease: Infantile and late infantile phenotypes (Krabbe disease) for inclusion on the Recommended Uniform Screening Panel (RUSP). We heard during the Thursday morning public testimony the devastating effects of the condition on children and their families, and we recognize the incredible effort by advocates, families, friends, clinicians, and scientists to gather the resources and do the work to bring the nomination to the Committee. We can only imagine how disappointed you must feel after more than a decade of working to bring Krabbe disease to this point. We would like to meet with you in the coming month to discuss key outstanding questions identified in the Committee deliberation. Once these questions are resolved, the Committee could consider an expedited review process (this would require approval by the Committee).

To recap the recent events, as you know the Committee requested a formal review of the scientific evidence by the External Evidence Review Workgroup (ERG) regarding screening, diagnosis, and follow-up care for Krabbe disease, using published data. You understand that the decision to go forward with the review reflects positively on the importance of the condition and on the status of test development and treatment evaluation, and some of you participated in the process through the Technical Expert Panel. The findings from the comprehensive and objective evidence review were presented and discussed by the Committee at the February 2023 meeting.

The Committee did not recommend to the Secretary the addition of Krabbe disease to the RUSP at this time. This was an extraordinarily difficult decision, and as indicated by the tie vote, different Committee members judged the evidence in terms of certainty and net benefit differently. Seven concluded that there is not sufficient evidence of significant net benefit to recommend population based NBS for Krabbe disease. We follow Robert's Rules of Order in the case of a tie vote, as we cannot assure that there will be an odd number of Committee

members participating in any vote, given that members may be absent or recuse themselves at any time.

As noted above, Krabbe disease can be reviewed by the Committee again for addition to the RUSP in the near future. For reconsideration, additional published data on the following topics would better equip Committee members to weigh net benefits:

- Evidence regarding efficacy of HSCT for early infantile Krabbe disease that (1) systematically reports outcomes and (2) adequately classifies cases as early vs. late onset (e.g. psychosine levels or genetic markers of infants transplanted).
- Evidence regarding harms of HSCT for infants transplanted in the first two months of life, including possibility of transplant of infants not meeting criteria for early infantile disease.
- Evidence regarding outcomes of infants who are at risk of late infantile Krabbe disease, as these children may experience even greater benefits than early infantile Krabbe disease; such evidence should include number lost to follow-up and potential burden on families and infants of intensive follow-up visits and consequences of indeterminate diagnostic testing.

The HRSA team will be contacting you to set up a meeting to discuss next steps. If you have any questions in the meantime, please contact me at achdnc@hrsa.gov.

Thank you again for your nomination of Krabbe disease for inclusion on the RUSP. I look forward to hearing from you soon.

Sincerely yours,

/s/

Ned Calonge, MD, MPH
Chairperson

ATTACHMENT:

Committee Representatives Presentation of Newborn Screening for Krabbe Disease
Evidence-Based Review of Newborn Screening for Krabbe Disease

Cc: Leticia Manning, MPH
Acting Designated Federal Official
Health Resources and Services Administration