Advisory Committee on Heritable Disorders in Newborns and Children

Advisory Committee on Heritable Disorders in Newborns and Children
5600 Fishers Lane, Room 18W68
Rockville, Maryland 20857
301-443-2521– Phone
www.hrsa.gov/advisory-committees/heritable-disorders

August 15, 2022

Megan Pesch, MD, MS, FAAP, President-Elect
National CMV Foundation
PO BOX 18322
Tampa, FL 33679

Dear Dr. Pesch:

The Advisory Committee on Heritable Disorders in Newborns and Children (Committee) appreciates your nomination of congenital cytomegalovirus (cCMV) for inclusion on the Recommended Uniform Screening Panel (RUSP). As part of the Committee's formal review process, a review of the nomination package was conducted by the Nomination and Prioritization Workgroup.

The Committee recognizes cCMV as a medically serious condition, with a CLIA-approved confirmatory test and available treatment modalities.

However, the Nomination and Prioritization Workgroup concluded that they had insufficient information to move the nomination forward in the process. One of the key requirements for all nominations is a prospective population-based pilot study. In order to make a decision as to whether to advance the nomination to the next step of evidence review, the Committee will require additional information in the following areas:

A. **Prospective Population-based Pilot Study** – Data from the pilot studies should address the following:
    - The pilot study should evaluate the newborn screening protocol in a manner that is similar to those utilized by state newborn screening programs with respect to the timing and approach to screening. The pilot studies described include point-of-care testing using saliva samples. Please provide additional information on how this approach could be implemented as population-based screening across states.

- The available pilot study data should include an analysis of the net benefits of clinical interventions following newborn screening identification compared to clinical diagnosis and treatment.

B. **Case definition** – The current case definition includes a high number of individuals who will be identified as a case but will remain asymptomatic. Please provide clarification regarding what is considered a cCMV case that requires treatment, beyond screening for hearing loss and developmental delay, and clinical management. The nomination should clearly indicate the number (proportion) of infants likely to benefit from population-based newborn screening, as compared with existing clinical practice (such as testing in response to symptoms).

C. **Characteristics of the screening test –** There is insufficient data and evidence indicating a viable high-throughput, highly specific, and sensitive screening test. It is unclear whether the proposed nucleic acid amplification tests using saliva samples to detect CMV are 1) feasible to implement; and 2) compatible with the existing newborn screening processes, e.g. the anticipated turnaround time for results given the large number of samples and number of samples to be processed in a given run.

D. **Clinical Utility –** Based on the data provided and the current case definition, CMV is a common infection and the screening will identify many cases. However, the nomination package was unclear regarding the benefit of a population-based screening. If there are any data available that describes the impact of screening, including the potential benefits of early identification and treatment and potential harms and burden of follow-up for those with benign cCMV infection, please provide in a package resubmission. It will be important to include evidence-based estimates of the proportion of individuals that will be expected to benefit by earlier diagnosis of complications and the magnitude of those expected benefits, compared to the proportion of individuals that will undergo the burden of the screening protocol with no expected benefit. This information is critical to understanding the "net benefit" of the proposed NBS protocol, which is the key element of the decision-making process.

E. **Treatments -** The recommended follow-up and treatment protocol is unclear. Please provide more information on whether there is a clear, recommended treatment protocol (e.g. which cases would receive antiviral medication vs. not, which cases would receive ophthalmological treatments and who would provide them) that could be implemented by the state newborn screening programs. Additional information on potential clinical outcomes that allow for tracking progress and outcomes of treatment would be helpful.

The Committee encourages you to resubmit the nomination when the above items have been addressed. Upon receipt of the completed nomination package, the Committee will review the updated nomination package to determine if the required information is present to enable consideration by the full Committee as to whether cCMV will move forward for a full evidence review.

If you have any questions about the additional information requested or when you are ready to submit an updated package, please contact me at achdnc@hrsa.gov.

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

Sincerely yours,

/s/

Ned Calonge, MD, MPH
Chairperson

ATTACHMENT: Summary of Nomination Requirements and Key Considerations

Cc: Soohyun Kim, MPH
Acting Designated Federal Official
Health Resources and Services Administration