Advisory Committee on Heritable Disorders in Newborns and Children

Advisory Committee on Heritable Disorders in Newborns and Children
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June 7, 2022

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). 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.

The Committee conducts a thorough review in order to provide evidence-based recommendations to you. On May 12, 2022, the Committee voted to send you the recommendation to add the nominated condition Guanidinoacetate Methyltransferase (GAMT) deficiency to the RUSP. This recommendation is based upon Committee deliberations and findings from the evidence-based review for GAMT deficiency, which includes detailed information on clinical data, testing methodology, available treatments, potential benefits and harms, an assessment of impact on the public health systems, and public comments.

GAMT is an enzyme needed to make creatine, which provides energy for cellular metabolism. GAMT deficiency is an autosomal recessive disorder that leads to low plasma and brain creatine levels and elevated concentrations of guanidinoacetate (GUAC) in the brain and cerebrospinal fluid, blood, and urine. The prevalence based on newborn screening data from Utah and New York is between 0.13 – 0.31 per 100,000 live births. Signs of GAMT deficiency (e.g., hypotonia, seizures, developmental delay) do not typically develop until after 3 months of age and clinical diagnosis is often

delayed. When untreated, the low levels of creatine and high levels of neurotoxic GUAC leads to severe and progressive neurological problems, including significant intellectual disability, limited speech development, recurrent seizures, behavioral problems, and involuntary movements.

Treatment for GAMT deficiency involves lifelong oral supplementation with creatine and ornithine, oral sodium benzoate, and a protein-restricted diet to reduce intake of arginine. This treatment is accessible and low-cost. Although GAMT deficiency is rare and there are limited data, available studies suggest that presymptomatic therapy is most often associated with normal neurological development and that treatment is likely associated with better neurological outcomes, cognitive development, and function.

The Committee deliberated on the net benefits, certainty of available evidence and feasibility of newborn screening for GAMT deficiency and determined that there is moderate certainty of significant benefits to infants identified with GAMT deficiency through newborn screening. There is a reliable screening test and screening, testing and treatment in state newborn screening systems are feasible. New York and Utah have incorporated screening for GAMT deficiency into their newborn screening programs using a laboratory-developed test with no reported missed cases to date. 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 for GAMT deficiency.

The Committee noted, until a commercial testing kit is available, some states will face challenges in method development and validating testing assays. In addition, given the burden on states to implement recently added and new RUSP conditions, the Committee recognized that, in reality, it may take longer than three years for states to fully implement GAMT deficiency screening.

After considering the available evidence, the Committee concluded that screening for GAMT deficiency will lead to significant benefits for infants born with this rare condition, their families and caregivers, and respectfully requests you accept the recommendation to add GAMT deficiency to the RUSP.

Sincerely,

/s/

Cynthia M. Powell, MD, FACMG, FAAP
Chairperson

Enclosure:
Report - *Evidence-based Review of Newborn Screening for Guanidinoacetate Methyltransferase Deficiency*

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