April 17, 2025

Dear Commissioner Cunningham,

On August 29, 2023, Shanna Quimby from Gavin Flying for a Cure, submitted a nomination to add metachromatic leukodystrophy (MLD) to Minnesota's newborn screening panel. On April 23, 2024, the nomination was presented to the Advisory Committee on Heritable and Congenital Disorders (also known as the Newborn Screening Advisory Committee) where advisors voted to create a workgroup to assess MLD's readiness as a condition for newborn screening here in Minnesota. This scientific workgroup met multiple times to discuss the literature and assess readiness specific to Minnesota. Their findings are documented in the Condition Readiness Criteria document enclosed.

On October 8, 2024, the workgroup's findings were presented back to the advisory committee. Members from the Public Health Laboratory also presented on current efforts and feasibility of screening for MLD. A few key elements of the advisor discussion are highlighted below.

- No U.S. based screening data available to analyze; uncertainty in translation of earlier specimen collection time in being able to pick up the target analyte.
- Without an available 2nd tier test (expected within the next 6 months), the number of false positives (211) would be significant as compared to the number of confirmed cases (0-1) based on available data from Germany.
- Arylsulfatase A (2nd tier test) is prone to false negative results, and we risk missing cases.
- Screening will likely pick up carriers and pseudodeficiencies.
- MLD is a condition with variable onsets and testing approaches have not proven a way to detect the early onset form, which is the form most likely to benefit from early identification and treatment.
- Diagnostic testing does not provide a clear answer of whether or not a newborn has MLD, even in individuals with clinical suspicion. Concern about lack of answers when screening the general healthy population and no phenotype to help.
- Treatment for the early onset form is gene therapy showing significant improvements, however, length of follow-up data is limited. Treatment available for all types cannot prevent all condition related morbidity and mortality.
- Consensus guidelines for management have been published.
- Cost and insurance coverage were discussed and concerns expressed about the accessibility of treatment and care for all individuals; treatment is ~4.35 million dollars and there is only one treatment center (University of Minnesota) in the entire state with known differences in coverage for public vs private and in-state vs out-of-state.

Following discussion, the Committee elected to proceed with a vote on the following:

To recommend the addition of metachromatic leukodystrophy to the Minnesota newborn screening panel.

No = 11

Yes = 8

With a majority vote, the recommendation did not pass. However, acknowledging the changing landscape and new information expected in the months to come, the Committee voted (12 yays to 4 nays) to reconvene the scientific workgroup and report back at the Spring 2025 meeting. A letter outlining the process, key discussion points, and outcome was provided to the nominator on October 29, 2024.

The scientific workgroup was reconvened on March 26, 2025 to review any new information and literature. Their findings are were presented at the advisor committee on April 15, 2025.

On April 15, 2025, these updated findings were presented back to the advisory committee. A few key elements of the discussion are highlighted below.

- Second tier testing will be available via the Mayo Clinic come June 2025.
- First tier screening will be translatable when comparing European and US data.

Following discussion, the Committee elected to proceed with a vote on the following:

To recommend the addition of metachromatic leukodystrophy to the Minnesota newborn screening panel.

No = 2
Yes = 16

With a majority vote, the recommendation passed.
Thank you for considering this information and recommendation when making your determination.

Sincerely,

/s/ Rae Blaylark

Rae Blaylark, Chairperson