Secretary's Advisory Committee on Newborn Screening Meeting

Friday, March 6, 2026

Report on the Nomination to Add Acid Sphingomyelinase Deficiency (Niemann-Pick Disease) to the Newborn Screening Panel in the State of Wisconsin

On March 14, 2025, the Secretary's Advisory Committee on Newborn Screening met via Zoom to discuss the nomination to add acid sphingomyelinase deficiency (ASMD) to the Wisconsin mandatory newborn screening (NBS) panel. ASMD was nominated by Jill Beirl from the National Niemann-Pick Disease Foundation and co-sponsored by Dr. Robert Steiner from the University of Wisconsin. The condition was previously considered by the Secretary's Advisory Committee on March 14, 2025, and the nomination was tabled due to inadequate information about the ability to differentiate between severe and more mild forms of ASMD on the screen, and inadequate information about the impact of treatment on the more severe acute neurovisceral forms. After obtaining this information, the Metabolic Subcommittee (October 17, 2025) and the Umbrella Committee (December 5, 2025) met and determined that ASMD meets all of the criteria for inclusion on the NBS. The Secretary's Advisory Committee met to discuss the nomination further.

ASMD, also known as Niemann-Pick types A, A/B, and B, is an autosomal recessive lysosomal storage disease that results in progressive multi system disease. It is caused by pathogenic variants of the sphingomyelin phosphodiesterase I (SMPD) gene that cause reduced lysosomal hydrolysis of sphingomyelin into ceramide and phosphocholine. This reduced activity leads to a buildup of sphingomyelin and

dysfunction within various tissues in the body. ASMD commonly affects the spleen, liver, lung, bone marrow, and lymph nodes, and the most severe forms of the disease affect the nervous system, including the brain

At the time of this report, three other states (Illinois, New Jersey, New York) screen for ASMD. There was discussion about why more states are not screening for this disorder if there is approved, effective treatment. The explanation is apparently due to competing priorities or the absence of an advocate, not due to uncertainty about the merits of screening.

Conditions added to the Wisconsin mandatory newborn screening panel must meet nine criteria. The committee considered each criterion in turn.

First, *mandated testing should be limited to conditions that cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening*. One study determined that patients with Niemann-Pick A (the severe early-onset neurovisceral form) experience symptoms within the first few months of life, typically organomegaly. Studies of patients Niemann-Pick A/B and Niemann-Pick B determined that the age of first symptom onset typically occurs within the first few years of life, but some patients did not develop symptoms until significantly later. Voting members agreed this criterion is met, 8-0.

Second, *for each condition, there should be information about the incidence, morbidity, and mortality and the natural history of the disorder*. ASMD is a very rare disease that is likely under/misdiagnosed. The incidence of ASMD is estimated to be between 0.25-0.6/100,000 births. With an annual birth count of 60,000 infants, Wisconsin can expect approximately 0-1 new diagnoses a year through NBS.

The severity of ASMD exists on a spectrum. Type A is associated with irritability, sleep disturbance, failure to thrive, hypotonia, severe gastrointestinal symptoms, and progressive respiratory symptoms. In one study of 10 infants, these symptoms contributed to a median time from diagnosis to death of 21 months, and none survived past the age of 3 years. Type B is associated with splenomegaly, hepatomegaly, bleeding, shortness of breath, pulmonary infections, joint/limb pain, bruising, headaches, diarrhea, below-average growth in childhood and bone fractures. Some of these patients develop neurologic abnormalities. In another study ASMD was reported to negatively impact a patient's physical functioning, self-esteem, social function, personal care and relationships. Voting members agreed this criterion is met, 8-0.

Third, *conditions identified by newborn screening should be linked with interventions that have been shown in well-designed studies to be safe and effective in preventing serious health consequences*. Individuals with the most severe form of ASMD typically develop symptoms around three months of age. At this stage of life respiratory and gastrointestinal symptoms have the greatest impact on patient health. Enzyme replacement therapy (ERT) has been shown to lead to significant improvements in lung disease, liver disease, growth velocity, and thrombocytopenia. Patients with the severe phenotype that were treated with a combination of enzyme replacement therapy and a fatty acid hydroxylase inhibitor had improved visceral disease and lifespan. However, this treatment can not change the neurodegeneration experienced by individuals with the severe form of ASMD. There are multiple companies currently working on treating the central nervous system form of the disease. There is potential for hypersensitivity related reactions, similar to what is expected for ERT in other disorders. ERT is approved for

treatment of non-central nervous system manifestations of ASMD for all three subtypes of the condition based on several robust clinical trials. Voting members agreed this criterion is met, 8-0.

Fourth, *the interventions should be reasonably available to affected newborns*. The FDA approved ERT for ASMD is widely available throughout the United States, and the National Niemann Pick Disease Foundation, in partnership with Sanofi's Care Connect Team, helps to support patients in accessing ERT through local infusion sites and providers. Insurance coverage for ERT has been consistently reported. Voting members agreed this criterion is met, 8-0.

Fifth, *appropriate follow-up should be available for newborns who have a false positive newborn screen*. Illinois has not detected a single false positive. This suggests that the test in conjunction with biomarker testing and genetic sequencing could have a false positive rate near zero. Voting members agreed this criterion is met, 8-0.

Sixth*, the characteristics of mandated tests in the newborn population should be known including specificity, sensitivity, and predictive value or other convincing medical evidence (experience, natural history, or literature).* There have not been any false positives detected in Illinois. This supports a very low false positive rate. Similarly, no false negatives have been reported. It is not presently possible to reliably determine which subtype is present at the time of testing. Voting members agreed this criterion is met, 8-0.

Seventh*, if a new sample collection system is needed to add a disorder, reliability and timeliness of sample collection must be demonstrated.* ASMD does not require a new sample collection system.

Eighth, *before a test is added to the panel the details of reporting, follow-up, and management must be completely delineated including development of standard instructions, identification of consultants, and identification of appropriate referral centers throughout the state/region*. The National Niemann-Pick Disease Foundation has an intake process available to all newly diagnosed patients. The foundation has also compiled a list of Comprehensive Care Centers that have the resources and experience to provide the recommended care to patients. There are metabolic centers in Madison and Milwaukee that can manage this disease and are familiar with it. Voting members agreed this criterion is met, 8-0.

Finally, *recommendations and decisions should include consideration of the costs of the screening test, confirmatory testing, accompanying treatment, counseling, and the consequences of false positives,* There should be minimal additional cost for the screening test as the Wisconsin State Lab already uses the platform that provides this test. Voting members agreed this criterion is met, 8-0.

As Acid Sphingomyelinase Deficiency was determined to fulfill all nine criteria, a motion was made to approve the nomination of ASMD. The motion to approve was seconded, then approved 8-0 by voting members.