

*Friday, March 6, 2026*

*Report on the Nomination to Add Gaucher Disease to the Newborn*

*Screening Panel in the State of Wisconsin*

On March 6, 2026, the Secretary's Advisory Committee on Newborn Screening met via Zoom to discuss the nomination to add Gaucher Disease to the Wisconsin mandatory newborn screening (NBS) panel. Gaucher Disease was nominated on August 21, 2025 by Sheldon Garrison, MD, a clinical researcher associated with Rogers Behavioral Health, Milwaukee Area Technical College, and co-sponsored by Michael Finkel, DO, MPH, a geneticist associated with the Medical College of Wisconsin. The Metabolic Subcommittee (October 17, 2025) and the Umbrella Committee (December 5, 2025) met previously and concluded that Gaucher disease meets all of the criteria for inclusion on the NBS.

Gaucher disease is an autosomal recessive lysosomal storage disorder caused by pathogenic variants in the *GBA1* gene encoding glucocerebrosidase enzyme. Deficiency of this enzyme leads to toxic accumulation of glucocerebroside lipids within multiple organs. This accumulation produces a multisystem disease including hepatosplenomegaly, pancytopenia, osteoporosis, and avascular necrosis. The severity of the manifestations varies depending on the disease type. Gaucher disease is classified as either non-neuropathic type 1, or neuropathic types 2 and 3 with type 2 being the most severe form. Clinical heterogeneity and the progressive onset of symptoms often lead to diagnosis delays/misdiagnosis.

At the time of this report, six states (Illinois, Missouri, New Jersey, Tennessee, New Mexico, and Oregon) currently screen for Gaucher disease. New York has a pilot program to gather information about Gaucher disease screening. 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.* Gaucher disease is a progressive lysosomal storage disorder that poses serious health risks beginning in infancy. Gaucher disease causes hepatosplenomegaly, pancytopenia, osteoporosis, and avascular necrosis to varying severity depending on the specific type. Type 1 is considered the non-neuropathic form while both types 2 and 3 have CNS involvement. Clinical heterogeneity and gradual symptom onset frequently lead to misdiagnosis and diagnostic delays preventing optimal treatment.. Patients with Gaucher type 1 may develop symptoms in childhood or later in life, and diagnostic delays can lead to missing the optimal window for intervention. Patients with Gaucher type 2 develop symptoms within the first months of life with a mean survival age of a year making early recognition important for treatment. Patients

with Gaucher type 3 typically develop symptoms in childhood and can also benefit from reduced diagnostic delays. 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.* The incidence of Gaucher disease in the general population is estimated to be approximately 1 in 50,000 births. Incidence is notably higher among the Ashkenazi Jewish population, estimated at 1 in 350 to 1 in 1,200. Screening programs around the United States have found incidence rates ranging from approximately 1 in 4,400 to 1 in 45,000. In Europe and North America approximately 90-95% of cases are non-neuronopathic type 1, with symptoms including growth retardation, splenomegaly, hepatomegaly, bleeding phenomena, and acute or chronic bone pain. Patients with type 2 represent fewer than 5% of all cases and develop early and severe neurological impairment in infancy, including hepatosplenomegaly, oculomotor paralysis, myoclonic epilepsy, and apnea, with a mean survival age of 11.7 months. Patients with type 3, representing approximately 5% of cases, develop neurological symptoms often before age 2, including progressive myoclonus epilepsy, cerebellar ataxia, spasticity, and dementia, with behavioral changes and unexpected death also reported; differentiating type 2 from type 3 remains clinically challenging and carries significant implications for management and family counseling. 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.* The standard treatment for patients with Gaucher disease is enzyme replacement therapy (ERT), approved by the FDA in 1994. Treatment of children with Gaucher disease has been shown to reduce hepatosplenomegaly and bone crises, increase hemoglobin levels and platelet counts, and normalize height/bone mineral density. These improvements in symptoms have led to reported improvements in patient quality of life. ERT is lifelong and most effective when initiated early. ERT does not impact the neurological progression of the disease. There are emerging therapies for Gaucher disease including brain-penetrant substrate reduction agents and pharmacological chaperones that show early promise in addressing neurological disease. Voting members agreed this criterion is met, 8-0.

*Fourth, the interventions should be reasonably available to affected newborns.* Enzyme replacement therapy is already administered at several locations across the state that have established infusion programs for lysosomal storage disorders. Coverage of treatments is widely accepted by payors throughout the country. 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.* The Wisconsin State Laboratory of Hygiene (WSLH) will communicate positive Gaucher disease results to the infant's primary care provider, and a clinical metabolic geneticist. The Gaucher Community Alliance recommends second-tier testing greatly as it greatly reduces the number of false positives. Infants with normal results on the second-tier testing will not be reported as screening positive. While

expected to be rare, parents of infants determined to be false positive will be offered genetic counseling to explain that their child is not at risk for this disease. Voting members agreed that, if second-tier testing is done, 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.* Screening for Gaucher disease uses measurement of GBA1 enzyme activity in dried blood spots via tandem mass spectrometry using a commercially available assay kit. Second tier testing uses measurements of lyso-GB1 on the same blood spot or sequencing of *GBA1*. New York has reported a false positive rate of 12% in the primary test. Oregon and New Mexico are currently using second tier testing if lyso-GB1. While their experiences have not been published, this approach is expected to produce a false positive rate near zero.

Seven members voted that Gaucher disease meets Criterion 6. One member wanted more information on how Wisconsin would implement second tier testing.

*Seventh, if a new sample collection system is needed to add a disorder, reliability and timeliness of sample collection must be demonstrated.* No new sample collection system is required; testing will utilize existing dried blood spots collected for current NBS assays.

*Eighth, before a test is added to the panel, the details of reporting, follow-up, and management must be completely delineated.* Follow-up for Gaucher disease will mirror existing protocols for metabolic conditions. The WSLH laboratory will report screening

positive results to the infant's primary care provider and metabolic specialist. The Gaucher Community Alliance (GCA) provides newly diagnosed patients with access to resources, education, and support. In Wisconsin, Children's Wisconsin/Medical College of Wisconsin, and the University of Wisconsin Hospitals and Clinics currently treat patients with Gaucher disease. Voting members agreed that this criterion was met by a vote of 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.* Adding Gaucher disease to the panel will add minimal cost for the Wisconsin state lab as they are already using the needed platform to test for other conditions. Treatment is covered by all payers and the GCA assists families with enrolling in support programs to cover costs not covered by insurance. Utilizing second tier testing is expected to reduce the number of false positives to near zero. Voting members agreed this criterion is met, 8-0.

A motion was made to approve the nomination of Gaucher disease on the condition that Wisconsin implements two tier testing. The motion to approve was seconded, then unanimously approved by voting members, 8-0.