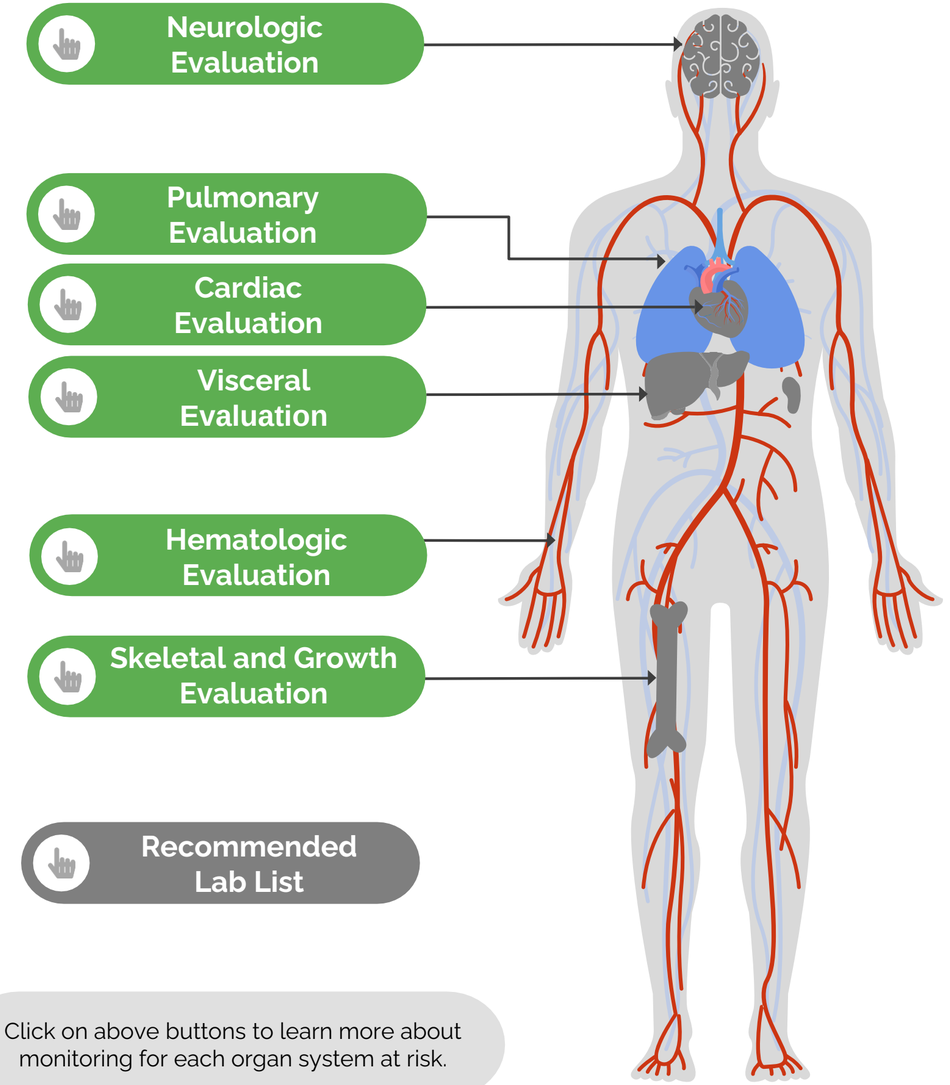
ASMD Monitoring and Management Recommendations[1,2]

Acid Sphingomyelinase Deficiency (ASMD) is a rare autosomal recessive disorder caused by pathogenic variants in the *SMPD1* gene. This results in deficient activity of the enzyme acid sphingomyelinase (ASM), a lysosomal lipid hydrolase required to degrade the sphingolipid, sphingomyelin, into ceramide and phosphocholine. Clinical features, age of onset and disease severity can vary greatly among the subtypes and even within families whose affected members have inherited identical genetic alterations.

Recommended Multidisciplinary Assessments of Patients with ASMD: Published clinical guidelines for the management and monitoring of ASMD have been developed by expert representatives from a range of professional groups including pediatric and adult metabolic specialists, geneticists, neurologists, hepatologists, pulmonologists, epidemiologists, clinical biochemists, specialist nurses and patient support group representatives. Patients with ASMD benefit from multidisciplinary and multi-professional follow–up from physicians and allied health care professionals with experience in ASMD. These specialists from different disciplines should work together to integrate information and care as much as possible. This tool was created based on those consensus guidelines.
Based on the patient's individual needs, health care providers will determine which assessments to perform and their required frequency.

General Evaluations	Frequency
Baseline History	
Establish natural history, systemic involvement, current level of disease severity, and estimate rate of progression	At Baseline
Interval History	
Establish rate of disease progression	3-12 mo
Physical Exam	
Document growth parameters	6-12 mo
Assess for neurological features and organomegaly	6-12 mo
Assess for fatigue, abdominal pain, and/or bleeding tendency*	6-12 mo
Family Support and Resources	
Assess need for family support and resources at each visit	6-12 mo
Assess need for community or online resources such as Parent to parent; social work involvement for parental support	6-12 mo
Assess for home nursing referral	6-12 mo
Assess for any change in social, domestic, or school or work related activities	6-12 mo



Click on above buttons to learn more about monitoring for each organ system at risk.

MAT-US-2403872 v2.0 - P
Expiration Date: 03/24/2028

Neurologic Evaluation

Clinical Examination and History At the time of diagnosis or symptom onset and at regular intervals (6-12mo)
Comprehensive neurologic evaluation, assess neurologic function, and frequency of headaches
Screen for age-appropriate developmental milestones
Assess for hypotonia, ataxia, and hyporeflexia
Monitor for development of peripheral neuropathy
Assess for chronic pain and fatigue
Evaluation of nutritional status and safety of oral intake* Educate family on progressive worsening of swallowing skills and increased risk of aspiration
Assess for sleep disturbance that can affect irritability and quality of life*

Assessments	Baseline and Frequency
Ophthalmology Evaluation	
Ophthalmoscopy to assess presence of cherry-red spots	Only at baseline
Developmental or Cognitive Evaluation	
Formal age and functionally appropriate developmental assessment (evaluation for early intervention/special education) using standardized assessment tools	As needed
Evaluation of cognitive impairment including motor, adaptive, cognitive and speech/language	Children: 6 mo Adults: 12 mo
Neuropsychiatric Evaluation	
Document psychiatric manifestations and response to therapy	6-12 mo as indicated
Swallowing Evaluation	
For patients with neuronopathic ASMD, swallowing assessment in all patients at risk* Document presence of dysphagia and for patients with neuronopathic ASMD*	Children: 6 mo Adults: 12 mo (if asymptomatic and stable disease)

*For patients with neuronopathic ASMD

MAT-US-2403872 v2.0 - P
Expiration Date: 03/24/2028

Pulmonary Evaluation

Clinical Examination and History At the time of diagnosis or symptom onset and at regular intervals (6-12mo)
Assess recurrent chest infections
Assess for shortness of breath
Auscultation

Assessments	Baseline and Frequency
Pulmonary function testing, including assessment of diffusing capacity*.	annually
O2 saturation	annually
Exercise tolerance*	annually
6 Minute Walk Test*	annually
Chest radiograph and/or high resolution chest CT to assess extent of interstitial lung disease	every 2–4 years

*In patients old enough to cooperate.

MAT-US-2403872 v2.0 - P
Expiration Date: 03/24/2028

Skeletal and Growth Evaluation

Clinical Examination and History At the time of diagnosis or symptom onset and at regular intervals (6-12mo)
Assess growth in children, anthropometric measurements in adults
Assess for fractures and/or extremity pain
Nutritional assessments

Assessments	Baseline and Frequency
Bone density studies	As clinically indicated
Document weight and linear growth in children	At least every 6–12 months,

MAT-US-2403872 v2.0 - P
Expiration Date: 03/24/2028

Visceral Evaluation

Clinical Examination and History At the time of diagnosis or symptom onset and at regular intervals (6-12mo)
Assess for degree of liver disease with labs and non-invasive imaging^
Review any history of for liver fibrosis, cirrhosis, portal hypertension, and variceal bleeding in adults
Assess for splenomegaly and hepatomegaly via physical exam

Assessments	Baseline and Frequency
Blood Investigations	
Serum chemistries including liver transaminases (ALT, AST), albumin, and clotting factors to evaluate for progression of hepatic dysfunction	At least annually
Imaging Studies	
Liver and spleen MRI including volumetric assessment*	As needed
Liver elastography or FibroScan to evaluate for hepatic fibrosis and cirrhosis	As needed

Click here for a recommended lab list

Clinical Considerations
Avoid splenectomy
Adult patients with transaminitis/ fibrosis/cirrhosis should be followed by hepatologist
Liver biopsy may be indicated with evidence of deteriorating liver function and non-invasive means to ascertain fibrosis are not available.
Patients with advanced cirrhosis should be monitored and treated for risk of gastrointestinal bleeding and surveillance for hepatocellular cancer.
Counsel family regarding the risk of contact sports to minimize trauma to the spleen
At initial evaluation of liver involvement, liver panels should include tests for ferritin, iron saturation, and viral and autoimmune serology to rule out potential co-morbidities

^ Use cautiously as this system is heavily based on elevated bilirubin, INR and creatinine, indicators that generally do not accurately reflect the extent of liver disease in ASMD
*Ultrasound can be performed in younger patients and where resource is limited.

MAT-US-2403872 2..0 - P
Expiration Date: 03/24/2028

Cardiac Evaluation

Clinical Examination and History At the time of diagnosis or symptom onset and at regular intervals (6-12mo)
Auscultation

Assessments	Baseline and Frequency
Cardiac Assessment (Adult Only)	
EKG,	Every 3-5 years
echocardiogram	Every 3-5 years
coronary angiogram as clinically indicated	Every 3-5 years
Baseline assessment of coronary artery status by HRCT or cardiac computed tomography for coronary calcium scoring in adults. Follow up imaging can be combined with HRCT for pulmonary monitoring or as clinically indicated	
Blood Investigations	
Measurement of lipid profile to evaluate for increased levels of triglycerides and total cholesterol, with low HDL-cholesterol levels	At least annually

Click here for a recommended lab list

Clinical Considerations
The use of lipid lowering therapy (e.g. statins) in ASMD patients as a primary prevention needs careful consideration in the context of the overall cardiovascular risk of the individual

MAT-US-2403872 v2..0 - P
Expiration Date: 03/24/2028

Hematologic Evaluation

Clinical Examination and History At the time of diagnosis or symptom onset and at regular intervals (6-12mo)
Assess for risk of bleeding
Assess for history of easy bruising and bleeding

Assessments	Baseline and Frequency
Blood Investigations	
Complete blood count to evaluate for thrombocytopenia, leukopenia, and anemia	At least annually
Coagulation profile	At least annually

Click here for a recommended lab list

MAT-US-2403872 v2.0 - P
Expiration Date: 03/24/2028

Recommended Lab List

Recommended Lab List
Liver enzymes/ hepatic function panel (transaminases, GGT, bilirubin, albumin)
Vitamin D 25-OH
Coagulation profile
Complete blood cell count (CBC)
Lipid profile
Biomarker: lyso-sphingomyelin
Albumin

GGT, Gamma-Glutamyl Transferase.

MAT-US-2403872 v2.0 - P
Expiration Date: 03/24/2028

References

1. Geberhiwot T, Wasserstein M, Wanninayake S, et al. Consensus clinical management guidelines for acid sphingomyelinase deficiency (Niemann-Pick disease types A, B and A/B). *Orphanet J Rare Dis.* 2023;18(1):85. Published 2023 Apr 17. doi:10.1186/s13023-023-02686-6

2. Wasserstein M, Dionisi-Vici C, Giugliani R, et al. Recommendations for clinical monitoring of patients with acid sphingomyelinase deficiency (ASMD). *Mol Genet Metab.* 2019;126(2):98-105.doi:10.1016/j.ymgme.2018.11.014

MAT-US-2403872 v2.0 - P
Expiration Date: 03/24/2028