Let's talk about alpha-mannosidosis

for healthcare professionals

A quick reference guide for healthcare professionals involved in the care of a patient with alpha-mannosidosis

This leaflet has been funded by Chiesi Global Rare Diseases and developed by Rare Disease Research Partners in collaboration with MPS Society UK, ISMRD, specialist clinicians and a metabolic nurse. Everyone involved received a fee for their consultancy advice.

ABOUT ALPHA-MANNOSIDOSIS (AM)

AM (OMIM 248500) is a **rare**, lysosomal storage disorder caused by mutations in the *MAN2B1* gene, resulting in a deficiency of the alpha-mannosidase enzyme.[1]

Prevalence: Estimated at 1:1 000 000 live births.[1]

Pathophysiology: Impaired glycoprotein degradation leads to systemic accumulation of mannose-rich oligosaccharides in cells, causing **progressive multisystem dysfunction**.[1,2]

Inheritance: Autosomal recessive.

Diagnosis: Diagnosis is usually established via measurement of alpha-mannosidase enzyme activity in leukocytes and/or genetic testing for pathogenic *MAN2B1* variants utilising either targeted gene sequencing or comprehensive genomic testing.[1]

MANAGING AM

Care should be led by a metabolic specialist or geneticist and involve coordinated input across multiple specialties. Key priorities include preventing complications (e.g. myopathy, ataxia, infections, hearing loss, cardiac/ respiratory/gastrointestinal issues, neuro-behavioural/ psychotic issues), supporting transitions between paediatric and adult services, and ensuring access to education, mental health, and community support.[1,3,4]

There is currently no cure for alpha-mannosidosis, but symptoms can be managed through supportive care to improve quality of life. Ongoing research continues to advance understanding of the condition. **For further information and guidance on management options, including specialised care, please refer to a specialist centre.**

On the next page you will find a list of the body systems that may be affected by AM, along with symptoms, complications and the medical specialties that can support your patient in obtaining appropriate care.

Disclaimer: This leaflet serves as a guide to help healthcare professionals who do not regularly treat patients with alpha-mannosidosis. It does not provide medical advice; please contact the patient's specialist centre with any concerns.

Symptoms and progression

Increased levels of oligosaccharides in urine may suggest AM.[2] Variable spectrum of clinical findings and progression depending on phenotype and age of onset. Most children show symptoms within the first decade.[1,2] Symptoms include facial and skeletal abnormalities, hearing loss, speech difficulties, muscular weakness, immunodeficiency, ataxia and cognitive impairment.[1,2]

KEY QUESTIONS TO ASK

- [ ] When did the symptoms of AM start?
- [ ] When did the patient receive a diagnosis of AM?
- [ ] What treatment is the patient receiving? For how long?
- [ ] In what areas can I assist with patient care (or care of the caregiver)?
- [ ] What are the contact details for the patients' AM specialist/specialist centre/healthcare team?
- [ ] What specialists are already involved in the patient's care?
- [ ] Do I need to make a referral?
- [ ] **Have the patient and family been referred to genetic counsellors to discuss the risk of being affected or being a carrier?**
- [ ] Have the patient and family been made aware of relevant support groups and/or mental health support services?

Regardless of severity, AM can impact the quality of life of the patient, their siblings and their caregivers in many ways, including their ability to live independently, socialise, attend school or find employment.

You can print or download this leaflet here:

If you live in the UK: MPS Society

If you live in the US: ISMRD

If you are unable to scan the QR codes, links are provided on page 2

RECOGNISING SIGNS AND SYMPTOMS OF AM[1,2,3,4] — WHO NEEDS TO BE INVOLVED?

Body system affected	Is your patient presenting with?	Specialties to involve
Ear, nose and throat Hearing	☐ Hearing loss: early-onset or congenital ☐ Recurrent otitis media/upper respiratory infections ☐ Swallowing problems ☐ Delayed speech development	Audiology Otolaryngology (ENT) Speech and language therapy (SLT)
Facial features	☐ Coarse facial features, frontal bossing, maxillary hypoplasia	Dentistry Maxillofacial
Immunological	☐ Recurrent infections especially in childhood (ENT or chest), reduced leukocyte function, low immunoglobulins, autoimmune features (e.g. lupus-like rash), increased susceptibility to pneumonia	Immunology Infectious diseases
Musculoskeletal	☐ Axial: scoliosis, kyphosis, spinal stiffness ☐ Peripheral: joint contractures/stiffness, ankle equinus, reduced range of motion, musculoskeletal pain, progressive loss of ambulation ☐ Craniofacial anomalies	Neurosurgery Orthopaedics Physiotherapy (PT) Occupational therapy (OT)
Neurological	☐ Motor: Delayed motor milestones, progressive ataxia, dystonia, poor balance, impaired coordination ☐ Pain or discomfort ☐ Seizures	Neurology Pain clinic PT OT
Ophthalmological	☐ Strabismus, visual tracking difficulties, corneal clouding in some cases, pigmentary retinal changes in advanced cases	Ophthalmology
Respiratory and sleep	☐ Recurrent lower respiratory tract infections, snoring, obstructive sleep apnoea, poor overnight oxygenation	Pulmonology Infectious diseases Sleep services
Cognitive	☐ Developmental delay, intellectual disability, dysarthria ☐ Psychiatric: behavioural concerns, confusion, delusions, hallucinations, anxiety, poor mental health, depression	Learning disability team Neurology/neuropsychology Paediatrics Psychiatry Psychology SLT

Further information

MPS Society UK: www.mpssociety.org.uk/conditions/related-conditions/alpha-mannosidosis
ISMRD: www.ismrd.org/glycoprotein-diseases/alpha-mannosidosis/
Delphi Consensus: www.pubmed.ncbi.nlm.nih.gov/39024860/

QR code links

If you live in the UK: www.mpssociety.org.uk/conditions/research/alpha-mannosidosis-patient-and-caregiver-resources
If you live in the US: www.ismrd.org/glycoprotein-diseases/alpha-man-test/#patientresources

1. Ficicioglu C, Stepien KM. Alpha-Mannosidosis. 2001 Oct 11 [Updated 2024 Jun 13]. In: Adam MP, Feldman J, Mirzaa GM, et al., GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. **2.** Malm D, Nilssen Ø. Alpha-mannosidosis. *Orphanet J Rare Dis.* 2008; 3:21. **3.** Malm, D, et al. The natural course and complications of alpha-mannosidosis-a retrospective and descriptive study. *J Inherit Metab Dis.* 2014;37(1):79-82. **4.** Guffon, N, et al. Monitoring and integrated care coordination of patients with alpha-mannosidosis: A global Delphi consensus study. *Mol Genet Metab.* 2024; 142(4):108519.

The MPS Society (www.mpssociety.org.uk), the Society for Mucopolysaccharide Diseases, is the only registered charity providing professional support to individuals and families affected by MPS, Fabry and related lysosomal conditions in the UK. We are committed to transforming lives through specialist knowledge, support and research, making sure anyone affected by these conditions gets to live the life they want.

ISMRD (www.ismrd.org), the International Society for Mannosidosis and Related Diseases, is an internationally focused not-for-profit organization whose mission is to advocate for families and patients. We are The International Advocate for Glycoprotein Storage Diseases. Our mission, through partnerships built with medicine, science and industry, is to seek, detect and cure these diseases while providing a global network of support and information.

Rare Disease Research Partners (www.rd-rp.com) is a wholly owned, not for profit subsidiary of the MPS Society. Its social objectives are to reinvest any surplus to support the mission of the MPS Society to transform the lives of patients through specialist knowledge, support, advocacy and research.

Job Code: UK-LAM-2500006; ALL_25_951. PP-RA-01224 V1.0.
Date of preparation: February 2026.