touch™ NEUROLOGY

Integrating treatment advances for alpha-mannosidosis into effective MDT care

Practice aid for the management of people living with alpha-mannosidosis

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Treatment needs may vary by clinical subtype and evolve along the lifespan of people living with AM

Initial signs and symptoms are not specific to the disease, leading to diagnostic delays (mean delay ~5 years)[1]

Clinical subtypes of AM[1–4]

Type 3 SEVERE[1–3]

Immediately recognized due to **skeletal abnormalities**

- Other key manifestations include
  - Progressive CNS involvement
  - Hepatomegaly
  - Myopathy
  - Coarse facial features
  - Developmental delay
- Obvious progression, early death

Type 2 MODERATE[1–3]

Clinically recognized ≤10 years of age

- Key manifestations include
  - Skeletal abnormalities
  - Myopathy
  - Hearing loss
  - Speech delay
  - Recurrent infections
  - Developmental delay
- Slow progression

Type 1 MILD[1–4]

Clinically recognized >10 years of age

- Key manifestations include
  - Hearing loss
  - Ataxia, muscular weakness
  - Psychiatric disorders
  - Cognitive impairment
- Slow progression

Consensus recommendations on coordinated care

2024 DELPHI consensus study on monitoring and integrated care[5]

Assessments in newly diagnosed patients

- Genetic testing
- Baseline assessments

Routine follow-up and care

- Behavioural/psychiatric
- Biochemical assays
- Cardiac function
- CNS manifestation
- Cognitive impairment
- Hearing assessments
- Immune function
- Muscular/motor function
- Ophthalmologic pathologies
- Patient-reported outcomes
- Skeletal abnormalities
- Other manifestations

Treatment-related follow-up and care

- ERT-related monitoring
- Post-HSCT monitoring
- Supportive care monitoring
- Integrated care coordination

Consensus statement on MDT care[5]

"Patients with AM should have a long-term multidisciplinary care team that includes an AM specialist to coordinate the team, as well as a group of specialists with expertise in each patient's specific disease manifestations"

Available disease-modifying therapies

ERT[6,7]

Infusion of exogenous functional enzyme that does not cross the blood–brain barrier

Velmanase alfa	**EU indication:** Treatment of non-neurological manifestations in patients with mild-to-moderate AM[8] **US indication:** Treatment of non-CNS manifestations of AM in adult and paediatric patients[9]
Benefits	Phase III data show improvements in biochemical and functional parameters[10]
Safety considerations	Administration may result in IRRs, including anaphylactoid reaction[8,9] IRRs may be mitigated by pre-treating with antihistamines, antipyretics and/or corticosteroids[8,9]

HSCT[11,12]

Transplant functional enzyme-producing cells, with healthy donor cell CNS engraftment

Benefits	Data are limited, but studies show HSCT attenuates CNS disease, and can alleviate neuropathology[11]
Safety considerations	Reports of GvHD, and cases of re-transplantation due to graft failure[12] Recipients are at higher risk for autoimmune haemolytic anaemia and pulmonary complications[8]

Abbreviations and references

Abbreviations

AM, alpha-mannosidosis; CNS, central nervous system; ERT, enzyme replacement therapy; GvHD, graft versus host disease;

HSCT, haematopoietic stem cell transplant; IRR, infusion-related reaction; MDT, multidisciplinary team.

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