

Guidance for the treatment of Alpha Mannosidosis

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1	May 2025	PPPN	PPPN	June 2025	20 June 2025
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Record of Amendments			
Edition No.	Amendment	Amended by & date	Authorised by & date
1	Change to wording around HSCT	PPPN 21 Nov 2025	PPPN 21 Nov 2025
1	Change to ERT eligibility	Authors May 2026	PPPN 19 June 2026

1.0 First line therapies:

1.1 Velmanase alfa (Lamzede)- enzyme replacement therapy (ERT)

1.2 Haematopoietic Stem Cell Transplantation (HSCT)

2.0 Choice of therapy

ERT: Treatment with velmanase alfa should be initiated in children and young people aged <18 years. Treatment may continue after the patient turns 18 years, provided it was started before age 18 years and remains clinically appropriate.

HSCT: HSCT are typically carried out in children < 5yrs but may be considered in older children on a case-by-case basis

3.0 ERT Dosage

The recommended dose of velmanase alfa is 1 mg/kg of body weight administered once a week via IV

4.0 Best supportive care/ Palliative and symptom control

Patients who are deemed too severely affected to benefit from specific therapy, or adult patients who opt not to have ERT, will be offered supportive care as appropriate.

5.0 Patient Group/Diagnosis

- All children and adults with a confirmed clinical, biochemical and genetic diagnosis of Alpha Mannosidosis
- Eligibility for disease specific ERT treatment under this guidance is restricted to children and young people aged <18 years who meet treatment criteria. However, where velmanase alfa has been initiated before the age of 18 years, treatment may continue into adulthood subject to ongoing clinical review and continued benefit.
- Patients need to be eligible for NHS Care.

6.0 Starting Criteria (one or more of the following)

Biochemical and genetic diagnosis of alpha mannosidosis

ERT:

Children and young adults <18 years,

HSCT:

Children <5 years but may be considered in older children on a case-by-case basis

7.0 Stopping Criteria / Exclusion Criteria

ERT:

- Rapid progression of the neurological complications
- Co-existing co-morbidities
- Frequently missed infusions and lack of therapeutic response
- Another life-threatening illness
- Patient is no longer eligible for NHS treatment

8.0 Supportive therapy:

Supportive therapy is important for all patients including those on ERT

9.0 Laboratory testing at diagnosis:

Serum oligosaccharides

Urine oligosaccharides

Enzyme activity for alpha mannosidase activity

Genetic testing

10.0 Monitoring and efficacy measures:

Monitoring:

Post HSCT: annually

On ERT: annually

Muscular/motor function:

- 6MWT or 3MSCT, SARA scale annually

Skeletal abnormalities:

- X-ray/CT/MRI as clinically indicated.
- DEXA scan/qCT as clinically indicated.

Cognitive function/neurological disease:

- Neuropsychology review as indicated.
- MRI brain, CT/EEG/cranial imaging as clinically indicated

Hearing/ENT:

- Audiometry annually or as clinically indicated
- ENT/airways assessment as clinically indicated

Behavioural/ neuropsychiatry:

- Neuropsychology/neuropsychiatry review as clinically indicated

Pulmonary involvement:

- Pulmonary function tests annually
- Overnight sleep study every 2 to 3 years as indicated

Immune function:

- Immunoglobulins, FBC, ESR and CRP annually
- Covid 19 vaccination annually

- Pneumococcal vaccination as clinically indicated

Cardiac involvement:

- ECG and echocardiography annually
- cardiac MR as clinically indicated

Ophthalmology:

- Eye assessment at diagnosis and 1-2 yearly

Other:

- Dental health review annually
- Hormonal dysfunction and endocrine disorders, growth problems annual review

Monitoring:

Serum/urine oligosaccharide testing annually

Antibody testing in patients treated with ERT as clinically indicated

Best supportive care:

Patients who are on supportive care only for the treatment of alpha-mannosidosis should be monitored every 6–12 months for symptom-based assessments.

11.0 Other cost reducing/saving measures (e.g. vial sharing, procurement etc)

Prescribed dose will be by weight unless SPC states otherwise.

For children (< 16 years) ERT dose will be calculated based on body weight and capped at a BMI that is increased +2SD above the median (98th centile) for age.

For adult patients with an increased BMI of 27 kg/m² consider capping ERT dose.

Vials will be used in integer units with alternating vials to ensure the most cost-effective use. No drug will be wasted. Where members of the same family are infused simultaneously in the same house the possibility for vial sharing will be explored.

12.0 Potential impact of stopping drug on patients & other measures needed (e.g. palliative care etc)

It is recommended that conversations regarding advanced care planning should be approached early. Discussions around ceiling of care and advanced decisions with the metabolic MDT and palliative care referrals need to be considered early where appropriate.

A mental capacity assessment should be considered for patients who are aged 16 years and older if there is reason to doubt capacity, and there is a decision to be made.

If it is deemed that the patient does not have capacity to make a specific decision, a best interest meeting is required with all those involved.

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