Guidance for the treatment of Mucopolysaccharidosis type I (MPS I)

EDITION NUMBER	2
DATE OF ISSUE	January 2020
REVIEW INTERVAL	Two years
AUTHORISED BY	
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Document review history						
Edition	**Review Date**	**Reviewed by**	**Authorized by**	**Date Authorized**	**Operative Date**	
1		EAG	Edmund Jessop		2010	
2	Jan 2020	HS LSD Centres	Joan Ward			

Record of Amendments			
Edition	**Amendment**	**Amended by & date**	**Authorized by & date**

1.0 First line therapies

1.1 Haematopoietic stem cell transplant (HSCT)

1.2 Enzyme replacement therapy (ERT)
Laronidase / Aldurazyme® (generic / commercial)

2.0 Choice of therapy

2.1 HSCT:
Children < 2.5 years with a DQ >70.

2.2 ERT:
(1) Adults and children not suitable for HSCT.
(2) Prior to HSCT, and continued afterwards until achievement of donor-engraftment.

2.3 Palliative / Symptom control:
Patients who are deemed too severely affected to benefit from specific therapy (HSCT or ERT), or adults who opt not to have ERT, will be offered supportive care as appropriate.

3.0 Haematopoietic stem cell transplant (HSCT)

Paediatric (<2.5 years) patients with MPS I who have little or no cognitive impairment (DQ > 70) should be considered for a HSCT.

4.0 Enzyme replacement therapy (ERT)

Laronidase / Aldurazyme®

100 U/kg/week in 100 mls normal saline for patients weighing <20 kgs
100 U/kg/week in 250 mls normal saline for patients weighing >20 kgs

5.0 Patient Group/Diagnosis

All adult and paediatric patients with a confirmed diagnosis of MPS1, fulfilling treatment criteria.

6.0 Starting Criteria

All patients with a confirmed diagnosis of MPS I, who do not have a contraindication to therapy (see sections 8.0 and 9.0) should be considered for treatment:

7.0 Monitoring and efficacy measures

All patients with MPS I should be given the opportunity to be followed up at a specialist LSD centre for regular monitoring and discussion of treatment options.

It is recognized that the clinical severity of patients with MPS I varies greatly – the investigations and frequency of investigations below serve as a guide only.

Laboratory testing

Patients	Measurement tool	Frequency
All patients	▪ Urine GAGs (goal: reduce and maintain) ▪ Antibodies (patients on ERT) ▪ Chimerism / enzyme activity (patients post-HSCT)	Annually

Hepatomegaly

Patients	Measurement tool	Frequency
All patients	Ultrasound (goal: reduce organomegaly and maintain)	Annually (until stable)

Pulmonary Involvement / Exercise tolerance

Patients	Measurement tool	Frequency
All patients (as appropriate for age and ability)	▪ 6MWT ▪ Timed get up and go ▪ FVC ▪ FEV1	Annually

Cardiac involvement

Patients	Measurement tool	Frequency
All patients	▪ ECHO (+ / - MRI) ▪ Blood pressure ▪ ECG (or Holter)	Annually

Neurological disease

Patients	Measurement tool	Frequency
All patients	▪ MRI brain, cord ▪ Cervical spine (flexion / extension) ▪ Neurophysiology (NCS eg. median,	At diagnosis and regularly as clinically

	ulnar)	indicated. Annual c-spine review.

Skeletal dysplasia

Patients	Measurement tool	Frequency
All patients	Joint imaging, spinal imaging DXA (bone mineral density)	As indicated

Opthalmology

Patients	Measurement tool	Frequency
All patients	Assessment by an ophthalmologist with experience in MPS eye involvement	Annually (or as clinically indicated)

ENT

Patients	Measurement tool	Frequency
All patients	Assessment to include: • Audiometry • Upper airways /tonsils / adenoids review • Overnight oxygenation / Sleep study • Tracheal imaging (HRCT)	Annually (or as clinically indicated) As indicated

Growth / weight

Patients	Measurement tool	Frequency
All patients	Anthropometry (weight, height, BMI)	Annually

Functional Health and Well Being

Patients	Measurement tool	Frequency
All patients (as appropriate for age and ability)	MPS-HAQ questionnaire	Annually

8.0 Exclusion criteria for starting MPS-specific therapy

- Patients with MPS I who are deemed too severely affected to benefit from MPS-specific therapy.
- The presence of another life-threatening illness or disease where the prognosis is unlikely to be improved by MPS-specific therapy.

9.0 Stopping Criteria (ERT)

Stopping ERT will be discussed with patients and carers and considered in the following circumstances:

- Intolerable and unavoidable adverse effects.
- Intercurrent illness, where either long-term quality of life or expected survival is such that the patient will gain no significant benefit from specific treatment for MPS.
- Continued progression of disease, despite optimal therapy - such that the patient is no longer considered to gain significant benefit from specific treatment for MPS.
- At the request of the patient, or properly allocated guardian acting in the patient's best interests, if the patient is properly deemed not competent.
- If the circumstances of the patient's lifestyle are such that sufficient compliance with treatment is not possible.
- If the health and wellbeing of medical and / or nursing staff are placed under significant threat as a result of the actions or lifestyle of the patient.
- Emigration of the patient outside the jurisdiction of the UK, when administration and funding of the treatment becomes the responsibility of Health Services in the new country of residence / domicile.

10.0 Other cost reducing/saving measures

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 the dose will be capped as for a BMI of 27 kg/m^2.

Vials will be used in integer units with alternating vials if needed to ensure the most cost-effective use. No drug will be wasted.

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

For patients stopping drug due to inability to receive intravenous therapy (or due to patient choice not to have therapy, monitoring will proceed as above.

For patients ceasing all MPS-specific therapy due to a life-threatening co-morbidity a full evaluation of supportive care requirements will be conducted and delivered in partnership with local primary and secondary care.

For patients ceasing MPS-specific therapy due to environment or failure of compliance patients should continue to be monitored by the specialist centre at 6 monthly intervals and the conditions leading them to stop therapy be re-evaluated to enable MPS-specific therapy to be recommenced at the first appropriate opportunity.

Appendix 1

Annual Guideline Audit Form

Date	
Specialist Centre	
Completing Physician	
Total Number NHSE MPS I patients	
New NHSE MPS I patients in review period	
Number of new NHSE MPS I patients commencing ERT	
Number of new NHSE MPS I patients having a HSCT	
Number of new patients stopping ERT (& reason for this)	