Guidance for the treatment of Mucopolysaccharidosis type II (MPS-II)

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Document review history					
Edition No.	**Review Date**	**Reviewed by**	**Authorised by**	**Date Authorised**	**Operative Date**
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4	May 2025	PPPN	PPPN	June 2025	20 June 2025

Record of Amendments			
Edition No.	**Amendment**	**Amended by & date**	**Authorised by & date**

1.0 First line therapies:

1.1 Enzyme replacement therapy (ERT)
Drug name: Idursulfase / Elaprase (Takeda /)

2.0 Choice of therapy

ERT:
(1) Male adults and children .
(2) Female patients with disease manifestation

3.0 Haematopoietic Stem Cell Transplant (HSCT)

Various forms of stem cell transplantation have been used in patients with MPS II, with variable outcomes, although no formal studies of efficacy are available. International experience suggests that this modality of treatment may play a role in patients who are predicted to have neuronopathic MPS II, in whom IV ERT is not expected to cross the blood-brain barrier, but who have not yet developed substantial central nervous system disease. As such, HSCT may be considered in young paediatric patients predicted to have severe central nervous system disease.

4.0 ERT Dosage

Idursulfase

500 micrograms/kg once weekly in 100ml normal saline.

Pre-medication at prescriber's discretion.

5.0 Patient Group/Diagnosis

All male adult and paediatric patients with a confirmed diagnosis of MPS-II, fulfilling treatment criteria. Female patients with disease manifestation. Patients need to be eligible for NHS Care.

Confirmed diagnosis requires evidence of elevated urinary glycosaminoglycans, deficiency of iduronidase-2-sulfatase, exclusion of multiple sulfatase deficiency, and identification of disease-causing *IDS* variant. Enzyme replacement therapy may be initiated prior to molecular genetic results if biochemical tests consistent with diagnosis.

6.0 Starting Criteria (one or more of the following)

1. **Paediatric male patients** with confirmed MPS II and any of the following should be considered for treatment:

a. All may be offered ERT, however if there is evidence of progressive and significant cognitive decline discuss whether appropriate to commence treatment
b. All pre-symptomatic individuals who are identified by screening following diagnosis in a symptomatic family member should be considered for treatment.

2. **Late-presenting (mild/attenuated) patients including adults** with confirmed MPS II should be considered for treatment if any of the following apply:
    a. Evidence of systemic (non-Central nervous system) disease with clinical impact including any of:
        i. Signs of upper airway obstruction.
        ii. Cardiorespiratory issues considered potentially responsive to enzyme replacement therapy.
        iii. Evidence of impaired endurance as measured by the 6 minute walk test (6MWT) distance.
        iv. Joint involvement – stiffness/arthropathy affecting quality of life
        v. Hepato/splenomegaly

3. **Female patients** with disease manifestation: treatment with ERT should be considered depending on clinical evidence of disease.

MDT treatment approach
- supportive care
Psychology
Palliative

7.0 Monitoring

All patients with MPS II should 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 II varies greatly – the investigations and frequency of investigations below serve as a guide only.

Urine GAGs

Patients	Measurement tool	Frequency
All patients	• Urine GAGs	6-12 monthly

Respiratory Involvement / Exercise tolerance

Patients	Measurement tool	Frequency
All patients (as appropriate for age and ability)	▪ 6MWT ▪ Functional Mobility Scale ▪ FVC ▪ FEV1	Annually
	▪ Sleep study	Clinically as indicated

Cardiac involvement

Patients	Measurement tool	Frequency
All patients	Assessment to include: ▪ Echocardiography ▪ Ejection fraction ▪ Presence of valve disease / aortopathy ▪ Blood pressure ▪ ECG (or other rhythm monitoring)	Annually (paediatrics) and annual-biannual (adults)

Neurological disease

Patients	Measurement tool	Time Frame
All patients	▪ Head circumference	Baseline & every 6-12 months
	▪ Brain MRI / CT ▪ Cranio-cervical junction imaging (flexion/extension radiograph and MRI)	Baseline & every 1-3 years as indicated
	▪ Neurophysiology (Carpel tunnel routinely, elbow if clinically indicated)	Baseline and Annually (or as clinically indicated)
	▪ Neuropsychometric assessment	Baseline and as clinically indicated in paediatric age range
	▪ EEG only if clinically indicated	

Orthopaedic disease

Patients	Measurement tool	Frequency
All patients	▪ Vitamin D, bone biochemistry ▪ DEXA bone mineral density if indicated eg pathological fracture	Annual As indicated
All patients	▪ Joint imaging as clinically indicated (hips and spine)	As indicated

Ophthalmology

Patients	Measurement tool	Time Frame
All patients	Assessment to include: • Visual acuity • Optic nerve health • Corneal pathology • Assessment for signs of raised intracranial pressure • Retinal dystrophy/ retinitis pigmentosa monitoring	Annually (or as clinically indicated)

AUDIOLOGY

Patients	Measurement tool	Time Frame
All patients	• Audiometry	Annually (or as clinically indicated).

ENT

Patients	Measurement tool	Time Frame

All patients	Assessment to include: • Airway assessment • May include Airway imaging • Adenotonsillar pathology (especially paediatric) • Sleep study may be indicated to inform assessment of sleep disordered breathing/ obstructive sleep apnoea.	Annually (or as clinically indicated). Baseline and prior to anaesthetic interventions Refer also to MPS Airway Guideline

Growth / weight

Patients	Measurement tool	Frequency
All patients	• Anthropometry	Every clinic visit

Functional Health and Well Being

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

8.0 Stopping Criteria (ERT)

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

1. Intolerable life-threatening infusion reactions not controllable.
2. Inability to perform intravenous cannulation by peripheral or central device
3. Patient is non-compliant with monitoring regimen preventing ongoing safe administration of therapy. Inter-centre agreement may be helpful. Safeguarding interventions to be explored.
4. Patient develops another life-threatening condition with predicted life expectancy less than 6 months
5. Patient is no longer eligible for NHS treatment
6. Patient has declined neurologically and there is agreement that treatment is no longer in the patients best interests

7. Pregnancy/breastfeeding (consider temporary cessation

9.0 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 (98^{th} centile) for age.

For adult patients with an increased BMI of 27 kg/m^2 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.

10. 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 unexpected supply or compliance issues 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.