

Guidance for the treatment of Mucopolysaccharidosis type IVA (MPSIVA)

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Record of Amendments			
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1			
2			

1.0 First line therapy:

Elosulfase alfa (Vimizim) weekly infusion

2.0 Choice of therapy**ERT: Adults and Children**

HSCT: Not practiced in the UK, but available as a therapeutic option elsewhere

3.0 ERT Dosage

The recommended dose of elosulfase alfa is 2 mg/kg of body weight administered once a week via IV

4.0 Patient Group/Diagnosis

- All adult and paediatric patients with a confirmed diagnosis of MPSIVA, fulfilling treatment criteria.
- Patients need to be eligible for NHS Care.

5.0 Starting Criteria (one or more of the following)

Clinical, biochemical and genetic diagnosis of Morquio syndrome
Good venous access

6.0 Stopping Criteria / Exclusion Criteria

1. Poor response to ERT
2. Recurrent severe adverse reactions to ERT despite attempts at medical management
3. Poor venous access/ faulty port
4. Co-existing comorbidities limiting treatment benefit
5. Disease severity at diagnosis too advanced to benefit from ERT
6. Patient and family wish to stop treatment
7. Poor compliance, other life limiting illness
8. Patient is no longer eligible for NHS treatment

7.0 Laboratory Diagnosis:

1. Enzyme activity in plasma, leucocytes or fibroblasts
2. Genetic testing
3. Urine keratan sulfate:
4. Where available, tandem mass spectrometry may be used to assess levels of urinary keratan sulphate prior to starting elosulfase alfa at baseline, annually and when clinically required

8.0 Monitoring and efficacy measures:**Respiratory involvement:**

-Pulmonary function tests (FVC and MVV) in children over 5 years of age, annually
-Respiratory rate and arterial oxygen saturation, annually

- Evaluation of gas exchange and respiratory function before any planned air travel, as clinically indicated.
- Overnight sleep study (polysomnography) every 3 years after the diagnosis

ENT/Airways disease:

- ENT and airways examination annually
- Fibreoptic nasendoscopy and pharyngolaryngoscopy examination at diagnosis and as clinically indicated thereafter.
- Thorax CT scan, preferably with 3D reconstruction, as clinically indicated
- Age-appropriate hearing test as a baseline, and annually
- Speech and language therapy, as indicated.
- Formal balance tests (vestibular function tests), as clinically indicated.

Peri-operative airways assessment:

- Pre-, intra- and post-operative care for all procedures requiring general anaesthesia, conscious or deep sedation, should be supervised by an anaesthetist with experience in treating patients with MPS and/or complex airway management.
- Procedures which involve surgery to the head, neck, spine or thorax should be covered by neurological monitoring of spinal cord function.
- The use of laryngeal mask airway (LMA) for shorter procedures, or intubation with a video laryngoscope or fibreoptic intubation is recommended, as clinically indicated.
- Tracheal resection is an option for patients with severe airways disease and individual cases must be discussed at a national MDT meeting.
- A temporary interruption in ERT for surgical procedures is recommended.

Endurance/exercise tolerance:

- 6MWT or 25-ft walk test, annually

Cardiac involvement:

- 12-lead electrocardiogram (ECG), echocardiography, blood pressure measurements, annually
- Longer ECG monitoring (prolonged Holter/event monitoring), as clinically indicated.

Neurological disease:

- Standard MRI of the cervical spine, as clinically indicated

Skeletal dysplasia:

SPINE:

- standing or sitting X ray of the cervical and thoracolumbar spine every 2–3 years thereafter, or sooner if clinically indicated
- MRI of the whole spine (in neutral position), annually or as clinically indicated
- Flexion/extension MRI of cervical spine may be needed to identify changes in spinal canal and spinal cord
- Flexion/extension computerised tomography (CT) of the craniocervical junction may be considered in patients with MPS IVA if MRI is not available or if general anaesthesia is not possible

HIPS and KNEES:

-an anteroposterior (AP) pelvis radiograph should be performed at diagnosis and as clinically indicated

Ophthalmology:

-Assessment, annually

Dental health:

-assessment, annually

Growth/weight:

Height, weight, BMI annually

Tanner pubertal stage (until maturity).

Monitoring:

uGAG/KS levels,

endurance testing (preferably 6MWT),

respiratory function (if age compatible),

growth, height and weight,

pain, ADL and QoL.

Adverse reactions:

-Due to the potential for hypersensitivity reactions with elosulfase alfa, patients treated in the clinical trial programme received antihistamine premedication, with or without antipyretics, 30 to 60 min prior to the start of the infusion.

- Patients with a with previous history of IARs, can be given additional premedication, such as H2 receptor blockers or montelukast sodium.

-IARs are generally managed by reducing the rate of administration or by temporarily interrupting the infusion plus administration of additional antihistamines, antipyretics, or for more severe react (for a 12–18-h period prior to infusion).

- Due to the risk of sleep apnoea in patients with MPS IVA, use of a non-sedating antihistamine is recommended.

-In the case of recurrent severe reactions, desensitisation and the use of steroid premedication could be considered before discontinuing therapy.

In such cases it is worthwhile documenting the TAb and NAb status.

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 (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.

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

Patients with severe MPS IVA should be counselled at diagnosis that despite the availability of ERT, the disease remains a progressive condition and it is likely that at some point ERT will cease to provide any additional benefit. The risk/benefit balance of treatment should be evaluated and discussed with the family annually. Families should be reassured that when this point is reached, cessation of ERT is unlikely to lead to more rapid deterioration. Timely and proactive involvement of palliative care services should be considered in these situations.

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

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