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Protocol for Mucopolysaccharidosis type II (MPS II)Patients Started on Elaprase® (idursulfase)

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Reviewed by:

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Background:

Definition: Mucopolysaccharidosis type II (MPS II) also known as Hunter syndrome is a rare, life-threatening X-linked lysosomal storage disease with pathologic manifestations in most organ systems and tissues.

Causes: The disease is caused by a defect in the gene coding for the lysosomal enzyme iduronate 2-sulfatase (I2S) (*IDS* gene); as a result, the cells of affected individuals are either unable to produce the enzyme or produce it in low amounts. This results in an inability of the lysosome to effect the stepwise degradation of the glycosaminoglycans (GAGs) dermatan sulfate and heparan sulfate, which are important constituents of the extracellular matrix, joint fluid, and connective tissue throughout the body. Because the disease is rare, and early symptoms can mimic other more common disorders, MPS II is often under recognized and diagnostic delays are common.[1]

Clinical features: The majority of patients are male; on rare instance heterozygous females manifest findings. Age of onset, disease severity, and rate of progression vary significantly among affected males. In those with early progressive disease, CNS involvement (manifest primarily by progressive cognitive deterioration), progressive airway disease, and cardiac disease usually result in death in the first or second decade of life. In those with slowly progressive disease, the CNS is not (or is minimally) affected, although the effect of GAG accumulation on other organ systems may be early progressive to the same degree as in those who have progressive cognitive decline. Survival into the early adult years with normal intelligence is common in the slowly progressing form of the disease. Additional findings in both forms of MPS II include: short stature; macrocephaly with or without communicating hydrocephalus; macroglossia; hoarse voice; conductive and sensorineural hearing loss; hepato-splenomegaly; dysostosis multiplex; spinal stenosis; and carpal tunnel syndrome.[1,2,3]

Diagnosis: usually by findings of high dermatan and heparin sulfate in urine mucopolysaccharide analysis. The diagnosis is confirmed by deficiency of the enzyme on dry blood spot or white blood cell and DNA molecular testing of *IDS* gene.

Treatment: includes symptom-based interventions, enzyme replacement therapy with Elaprase® (idursulfase) and hematopoietic stem cell transplantation (particularly very young, severely affected patients). [1,2,3]

Purpose: The purpose of this policy is to dictate the management of patients with Mucopolysaccharidosis type II (MPS II) who are eligible for enzyme replacement therapy.

Baseline assessments and investigations prior to initiation of enzyme replacement therapy(ERT)[3,6-8]:

- Height, Weight, Head circumference
- Blood pressure
- Enzyme activity level
- DNA molecular testing for *IDS* gene
- IgG antibody test
- CBC, diff
- Chem1
- Liver enzymes
- CPK level
- Bone profile and vitamin D levels
- Urine for mucopolysaccharides
- Urine analysis
- Neurology evaluation
- MRI of brain and spine
- Median nerve conduction velocity
- Cognitive testing (developmental quotient (DQ) or intelligence quotient (IQ)
- ENT evaluation (audiometry and ABR test)
- Ophthalmology evaluation(visual acuity, retinal examination, corneal examination)
- Respiratory evaluation (Chest X-ray, forced vital capacity, forced expiratory volume, sleep study)
- Cardiology evaluation (ECG, Echocardiogram)
- Skeletal survey
- Abdominal CT or MRI to determine the spleen and liver volume. If not available, then, abdominal ultrasound.
- Functional outcome measurements: MPS Health Assessment Questionnaire, or other tools exploring functional ability and quality of life.
- 12 minutes' walk test (12MWT) and 3 minutes stair climb (3MSC)

Enzyme replacement therapy(ERT) administration protocol:

Premedication (1 hour prior to ERT infusion) with:

- Acetaminophen (10-15 mg/kg) PO; _____ (mg) PO.
- Diphenhydramine (1mg/kg) IV; _____(mg) IV.
- Methylprednisolone (1mg/kg) IV; _____ (mg) IV.

➢ Elaprase® (Idursulfase)[4,5]

- **Dose:** 0.5 mg/kg IV once weekly.
- **Strength:** 3ml (6mg/3ml), single use vial.
  Please round the dose up to the nearest whole vial in order not to waste any amount of the enzyme. For example if the patient Weight 10 kg give 6 mg instead of 5 mg.
- **Weight:** _____(kg): **calculated dose** _____(mg) IV.

- **Dilution:**
  - Dilute in 100 mL normal saline

Special Precautions:

- **Stable only in Normal Saline.**
- The diluted Elaprase® solution should be filtered through a 0.2 µm, low protein-binding, in-line filter during administration to remove any visible particles.

Infusion rate:

- Initial rate of 8 mL/hour for the first 15 minutes. If tolerated, may increase rate by 8 mL/hour increments every 15 minutes; maximum infusion rate of up to 100 mL/hour.
- Rate may be decreased, temporarily stopped, or discontinued based on tolerance.
- Initial infusion should be over 3 hours; if tolerated, subsequent infusions may be gradually reduced to a 1-hour infusion. Total infusion time should not exceed 8 hours.[5]

Nurses: Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Elaprase® infusion.

Undesirable effects: most common are infusion-related reactions; headache, hypertension, flushing, nausea, vomiting, diarrhea, abdominal pain, dyspepsia, infusion site reactions, Wheezing, dyspnea, Urticaria, rash, pruritus.

Note:

- If anaphylactic or other severe allergic reactions occur, immediately discontinue the infusion of Elaprase® and initiate appropriate medical treatment.
- If an infusion reaction occurs, regardless of pre-treatment, decreasing the infusion rate, temporarily stopping the infusion, or administering additional antipyretics and/or antihistamines may ameliorate the symptoms.

Monitoring the response to enzyme replacement therapy[3, 6-8]:

	Every 6 months	Every 12 months	Every Other Year
General			
Medical history Physical examination General appearance	**X**		
Lab test			
CBC, diff Electrolytes Liver enzymes CPK level Bone profile and vitamin D levels	**X**		
IgG antibody test		**X**	
Neurology			
MRI of brain and spine			**X**
Median nerve conduction velocity			**X**
Cognitive testing (developmental quotient (DQ) or intelligence quotient (IQ)		**X**	
ENT evaluation (audiometry and ABR test)		**X**	
Ophthalmology evaluation(visual acuity, retinal examination, corneal examination)		**X**	
Respiratory evaluation (Chest X-ray, forced vital capacity, forced expiratory volume, sleep study)		**X**	
Cardiology evaluation (ECG, Echocardiogram)			**X**
Skeletal survey			**X**
Abdominal CT or MRI to determine the spleen and liver volume. If not available, then, abdominal ultrasound.			**X**
Functional outcome measurements: MPS Health Assessment Questionnaire, or other tools exploring functional ability and quality of life.		**X**	
12 minutes' walk test (12MWT) and 3 minutes stair climb (3MSC)		**X**	

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