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Protocol for Mucopolysaccharidosis type VI (MPS VI)Patients Started on Naglazyme® (Galsulfase)

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Protocol for Mucopolysaccharidosis type VI (MPS VI) patients started on Naglazyme® (Galsulfase):

Background:

Definition: Mucopolysaccharidosis VI , also known As Maroteaux–Lamy syndrome, is a clinically progressive disorder with a spectrum of mild to severe phenotypes.[1-3]

Causes: The disease is caused by a deficiency in the lysosomal enzyme N-acetyl-galactosamine-4-sulfatase (also known as arylsulfatase B, ASB) due to a defect in *ARSB* gene coding for that enzyme; 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, 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 VI is often under recognized and diagnostic delays are common.[1-3]

Clinical features: Patients with rapidly progressing disease often have short stature with coarse facial features, joint and skeletal abnormalities, spinal cord compression, compromised cardiovascular and pulmonary function, corneal clouding, recurrent respiratory and ear infections, and early mortality in the late teens to early twenties, often from cardiopulmonary failure. MPS VI patients present with classical symptoms by 6–24 months of age. Although symptoms may appear later in life in those with slowly progressing disease, these patients nonetheless demonstrate severe morbidity and early mortality by the third to fifth decade of life. The patients often require clinical interventions related to one or more organ dysfunction such as corneal transplants, cardiac valve replacement, hip replacement, or spinal cord decompression surgery by their late teen to adult years. Although MPS VI patients do not typically exhibit neurocognitive deficits, physical limitations particularly with decreased sight and hearing can affect learning and development.[1-3]

Diagnosis: Usually by findings of high dermatan 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 *ARSB* gene.[1-3]

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

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

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

- Height, Weight, Head circumference
- Blood pressure
- Enzyme activity level
- DNA molecular testing for IDUA 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.

➢ **Naglazyme® (Galsulfase)**[4,5]

- **Dose:** 1 mg/kg IV once weekly.
- **Strength:** 5ml (5 mg/5ml), single-use vials.
  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 14 kg give 15 mg instead of 14 mg.
- **Weight:** _____(kg): **calculated dose** _____(mg) IV.

- **Dilution :**
  - For patients ≤ 20 kg – dilute in 100 mL normal saline
  - For patients >20 kg – dilute in 250 mL normal saline

Special Precautions:

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

Infusion rate:[4,5]

For less than or equal 20 kg:

- 3 mL/hour for the first hour. If the infusion is well tolerated, the infusion rate can be increased to 32 mL/hour for approximately 3 hours.

For more than 20 kg:

- The initial infusion rate should be 6 mL/h for the first hour. If the infusion is well tolerated, the rate of infusion may be increased to 80 mL/h for the remaining 3 hours.

The total volume of the administration should be delivered in no less than 4 hours.

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 Naglazyme® infusion.

Undesirable effects:

Most common: headache, fever, arthralgia, vomiting, upper respiratory infections, abdominal pain, diarrhea, ear pain, cough, and otitis media. Others: anaphylaxis and allergic reactions, infusion-related reactions.

Note:

- If anaphylactic or other severe allergic reactions occur, immediately discontinue the infusion of Naglazyme® 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]:

	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**		
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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