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Protocol for Pompe Disease Patients Started on Myozyme® (Alglucosidase Alfa)

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Reviewed by:

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Protocol for Pompe Disease patients started on Myozyme® (Alglucosidase Alfa):

Background:

Definition: Pompe disease or Glycogen storage disease type II (GSD-II), is a rare autosomal recessive disease. It is one of lysosomal storage diseases.[1]

Causes:

It is caused by the deficiency of acid a-glucosidase (GAA), which is needed for the degradation of lysosomal glycogen.[1-4]

Classification:

It is classified into 3 major subtypes depends on the age of onset:

- Classic infantile
- Juvenile
- Adult

Clinical Features: the classic infantile form usually present within 1st month of with hypotonia, and hypertrophic cardiomyopathy. Additional clinical features include: glossomegaly, motor delay, high CK level, elevated liver enzymes and hepatomegaly. Patient may die from cardiopulmonary failure or aspiration pneumonia without reaching 1 year of age. The juvenile form is characterized by predominant skeletal muscle dysfunction with motor and respiratory problem but rarely cardiac involvement. Calf hypertrophy can be present mimicking Duchenne muscular dystrophy. Myopathy and respiratory insufficiency deteriorate gradually and patient become dependent on ventilator or wheelchair. The adult form develop in 3rd or 4th decade and affect the trunk and proximal limb muscle. Involvement of diaphragm is frequent and acute respiratory failure may be the initial symptom in some patients.[1-4]

Diagnosis: The diagnosis is confirmed by deficiency of the enzyme on dry blood spot or white blood cell or fibroblasts or muscles and DNA molecular testing of *GAA* gene.

Treatment: In 2006, enzyme replacement therapy (ERT) for Pompe disease (Myozyme®) was approved in the USA, Europe, and Canada, with subsequent approval in countries around the world.[1-4]

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

Baseline assessment and investigations[5,6]:

- Height, weight, head circumference
- Blood pressure, heart rate
- Cognitive and developmental assessment
- Motor assessment using Alberta Infant Motor Scales (AIMS), Peabody Developmental Motor Scale-2 (PDMS-2), Pediatric Evaluation of Disability Index (PEDI), and Pompe PEDI
- ECG and Echocardiogram
- ECG holter montoring
- Chest X ray and spine X ray
- Pulmonary function test (only above 6 year of age)
- ENT evaluation (audiometry and ABR test)
- A videofluoroscopic swallowing assessment and gastroesophageal reflux evaluation
- CBC, diff
- Electrolytes
- Liver enzymes
- CPK level
- Bone profile and vitamin D levels
- Enzyme assay in dry blood spot or white blood cells.
- CRIM status determination in blood [collected by special tube from Genzyme company BD Vacutainer® CPT™ (Cell Preparation Tube) with Sodium Citrate, 4 mL should be extracted an (Becton Dickinson), stored at room temperature (18-25ºC) and protected from light, CPT tube should be mixed by inversion 8-10 times after blood draw and centrifuged at 1800 xg for 30 minutes before shipping and the supernatant colour is a pale yellow].
- Anti-rhGAA Antibody Evaluation
- Skin fibroblasts for CRIM status
- DNA molecular testing for GAA to predict CRIM status.

Enzyme replacement therapy(ERT) administration protocol:

For immune modulation protocol see appendix 1.

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.

➢ Myozyme®: Alglucosidase alfa.[7,8]

- **Dose:** 20mg/kg IV every 2 weeks.
- **Strength:** 50mg (5mg/ml), 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 4 kg give 100 mg instead of 80mg.

- **Weight:** _____(kg): **calculated dose** _____(mg) IV.

- **Dilution:**
  - For patients <10 kg – dilute in 50 Ml normal saline
  - For patients >10 kg – dilute in 100 Ml normal saline
  - Range: 0.5 – 4mg/ml. (Total volume will depend on dilution chosen)

- Dilution preferred_____, total volume _____(ml).[7,8]

Special Precautions:

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

Infusion rate:

- 1 mg/kg/hr x 30 min; _____mg/hr, _____ml/hr.
- 3 mg/kg/hr x 30 min; _____mg/hr, _____ml/hr.
- 5 mg/kg/hr x 30 min: _____mg/hr, _____ml/hr.
- 7 mg/kg/hr until complete _____mg/hr, _____ml/hr.

The total volume of the administration should be delivered in approximately 3-4 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 Myozyme® infusion.

Side Effect: anaphylaxis and allergic reactions (during & up to 3 hours after infusion), risk of acute cardio-respiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions (during and up to 2 hours after infusion), and immune mediated reactions.

Note:

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

The definition of effective treatment is:

An improvement in or a prevention of progression of disease activity as indicated by stabilization in clinical condition associated with an improvement in the abnormalities present at baseline. This is defined as improved cardiac response by echocardiography and ventilator-free survival within 12 weeks of therapy.[5,6]

Discontinuation of treatment:

a) If the patient develops a life-threatening complication unlikely to benefit from further ERT. This includes severe infusion-related reactions that are not controlled with adequate and appropriate medication.

b) Failure to comply with recommended dose regimen or follow up clinic visits and/or investigations.

c) Non-responsiveness to ERT as assessed by echocardiography at 24 weeks after starting treatment.[5,6]

When to start Immune modulation therapy?

- CRIM-negative patients
- The team agreed to start immune modulation protocol for any patient diagnosed with Pompe disease as all documented cases in Saudi Arabia so far is CRIM-negative.

Monitoring the response to enzyme replacement therapy:[5,6]

	Assessment	Frequency
Physical examination	Height/length, weight, head circumference, blood pressure, heart rate	every visit
Cardiac evaluation	ECG and echocardiography	2, 8, and 12 and 24 weeks and then every 6-12 month
	Holter monitoring	6 weeks, 12 weeks, 24 weeks, and then yearly
Respiratory evaluation	CXR	6 month and 12 month, then as clinically indicated
	Pulmonary function tests	Every 6 months
ENT evaluation	Audiometry and ABR test)	Every 12 month
Swallowing assessment	A videofluoroscopic evaluation, upper GI study and milk scan	As clinically indicated
Laboratory tests	CK, liver enzymes bone profile, CBC diff, electrolytes and vitamin D level	Every 3-6 month
	Anti-GAA antibody titers	Every 3 month unless CRIM negative or if immunomodulatory therapy has been used
Cognitive and developmental assessments	Denver Developmental screening test II, Bayley Scales of Infant and Toddler Development III	6 month, 12 month, then, yearly
Motor assessments	Alberta Infant Motor Scales (AIMS), Peabody Developmental Motor Scale-2 (PDMS-2), Pediatric Evaluation of Disability Index (PEDI), and Pompe PEDI	Every 6 month

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