Point-of-Care Resource for Healthcare Teams That Provide Care to Patients with Long-Chain Fatty Acid Oxidation Disorders (LC-FAODs)*

I. Understanding Long-Chain Fatty Acid Oxidation Disorders (LC-FAODs)

a. Definition and Characteristics
- Group of rare genetic metabolic disorders affecting the body's ability to break down long-chain fatty acids into energy.[1]
- Characterized by deficiencies in specific enzymes required for fatty acid oxidation, leading to an accumulation of long-chain fatty acids in the body, which can cause serious health issues such as muscle weakness, cardiomyopathy, liver dysfunction, and hypoglycemia.[1,2]
- Symptoms are typically induced by fasting, exercise, illness, or stress.[1]

b. Impact on Patient Quality of Life
- Patients often suffer from chronic fatigue, muscle pain, and recurrent rhabdomyolysis episodes, significantly impacting their daily lives and overall well-being.[1]
- The complex dietary adjustments required for managing LC-FAODs also have profound effects on both patients and caregivers.[3]
- These challenges necessitate frequent interactions with healthcare providers and can lead to frequent hospitalizations, imposing substantial emotional and financial burdens on patients and their families.[3]

II. Triheptanoin Therapy

a. Role in LC-FAOD Treatment
- Triheptanoin is an odd-carbon, medium-chain triglyceride (MCT) that serves as an alternative source of calories and fatty acids for patients with LC-FAODs.[4]
- Has an anaplerotic effect, meaning it replenishes intermediates in metabolic cycles, thereby increasing energy production.[4,5]
- Significantly reduces the yearly rates of major clinical events like rhabdomyolysis, hypoglycemia, and cardiomyopathy.[4]

b. Indications
- Patient Selection Criteria
  - Approved for adults and children with a molecularly confirmed diagnosis of LC-FAOD.[7]
  - Must not be used concurrently with any other MCT.[7]

c. Recommended Dosage and Administration
- Target: Up to 35% of total daily caloric intake (DCI), divided into at least 4 doses and administered at mealtimes or with snacks every 3-4 hours.[7]
- New patients: Start at approximately 10% of their DCI, divided into 4 doses per day. Increase the total daily dosage by approximately 5% DCI every 2 to 3 days until reaching the target dosage.[7]
- Switching from other MCT products: Discontinue the previous MCT product(s) before starting triheptanoin. Begin triheptanoin at the last tolerated daily dosage of MCT, divided into 4 doses per day, and increase by 5% DCI every 2-3 days until reaching the target dosage.[7]

d. Monitoring and Safety Considerations
- Adverse Reactions and Precautions
  - Common adverse reactions include gastrointestinal symptoms, eg, abdominal pain, diarrhea, vomiting, and nausea.[7]
- Drug Interactions and Contraindications
  - Avoid combining with pancreatic lipase inhibitors, eg, orlistat.[7]

III. Patient Education and Counseling

a. Lifestyle Modifications and Dietary Consideration in LC-FAODs
- Dietary guidelines:
  - Limit fasting to 8-10 hours (shorter for infants) to prevent metabolic decompensation.[1,8,9]
  - Keep dietary long-chain fats to 20%-30% of total energy intake.[1,9]
  - Use MCTs to safely boost energy levels.[9]
  - Increase carbohydrates moderately to meet daily caloric needs.[1,9]
  - Maintain protein intake at 25%-28% of daily calories to preserve muscle mass.[9]
  - Include small amounts of essential fatty acids to prevent deficiencies.[10]
  - Exercise and Illness:
    - Small, frequent meals and snacks are essential, especially before physical activity or at bedtime.[9]
    - Before strenuous activity, consider MCT oil, additional carbohydrates, and fluids.[1]
    - During illness or rhabdomyolysis signs, increase fluid and calorie intake.[1]

b. Symptoms and Complications of LC-FAODs.[11,12]
- Chronic Symptoms:
  - Fatigue
  - Muscle pain, cramps, and/or weakness
  - Cognitive fog
  - Hypotonia (decreased muscle tone)
  - Retinopathy (damage to the retina of the eyes)
  - Peripheral neuropathy (nerve damage outside the brain and spinal cord)

- Acute Symptoms:
  - Can lead to metabolic crises, hospitalization, or sudden death
  - Triggered by illness or fasting (may occur spontaneously)
  - Symptoms include:
    - Hypoglycemia (low blood sugar)
    - Rhabdomyolysis (muscle breakdown)
    - Cardiomyopathy (heart muscle damage)
    - Neurologic distress in infants and young children (extreme sleepiness or coma)
    - Changes in heartbeat
    - Muscle weakness
    - Appetite changes
- Management of Acute Metabolic Crises
  - Emergency glucose is needed to prevent muscle damage when fatty acids cannot be utilized.[12]
  - Glucose infusion amounts vary based on enzyme activity, age, and stress levels; no consensus on doses.[12]
  - Normoglycemia does not prevent catabolic crises; rhabdomyolysis can occur without low blood sugar, requiring ongoing glucose administration.[12]
  - Manage hyperglycemia with insulin, not reduced glucose intake.[12]
  - Monitor and supplement sodium and potassium levels; use antipyretics for fever.[13]
  - Plasma creatine kinase is the recommended marker for monitoring rhabdomyolysis, but symptoms often appear hours before detectable increases.[12]

IV. Additional Resources and Support

a. Patient Advocacy Groups
- INFORM Families
- MitoAction
- MitoCanada
- Patient Access Network (PAN) Foundation - LC-FAODs
- Saving Babies Through Screening Foundation
- The Metabolic Foundation

b. Educational Materials and Online Communities
- Fatty Acid Oxidation (FOD) Support
- International Network for Fatty Acid Oxidation Research and Management (INFORM)
- MitoAction
- VLCAD Nutrition Management Guidelines

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*This resource has been designed to be used by healthcare professionals to educate patients about long-chain fatty acid oxidation disorders and use of triheptanoin therapy.