**LETTER OF MEDICAL NECESSITY: MSUD**

**Date:**

**Patient:**

**D.O.B:**

**Policy Number:**

To Whom It May Concern:

This letter of medical necessity is regarding the nutrition management of **[PATIENT NAME].** This patienthas an inborn error of metabolism, a genetic disorder, known as **Maple Syrup Urine Disease (MSUD) (ICD 10: E71.0)** and is being followed in the genetic/metabolic clinic of **[CLINIC NAME].** This letter is to request coverage of **[CAMBROOKE PRODUCT NAME]** a medical food/formula(s) used for the treatment of MSUD.

MSUD results from a deficiency of an enzyme complex responsible for metabolizing the essential amino acids isoleucine, leucine, and valine. This deficiency results in the toxic build-up of the three amino acids and their byproducts in the body. MSUD is part of the newborn screening profile due to the devastating effects if undiagnosed or untreated. A patient with untreated MSUD will suffer irreversible brain damage, cerebral edema, coma, as well as severe and progressive neurological disorders and even death can occur if not treated promptly. Normal growth and development are possible if an infant with MSUD is treated appropriately immediately upon diagnosis. However, these patients remain at high risk for developing episodes of metabolic crises with that can be triggered by infection, injury, failing to eat, or even psychological stress. During these episodes these is a rapid, sudden spike in amino acid levels necessitating immediate medical intervention and usually hospitalization.

The three primary goals of treatment are:

1. To maintain blood levels of isoleucine, leucine, and valine to reduce toxicity to the brain
2. To ensure that energy intake is sufficient and sustained throughout the day to prevent fasting and breaking down of body proteins
3. To ensure that the individual’s overall nutritional requirements are met, allowing for normal growth and development and the avoidance of nutritional deficiencies

Currently, there is not an effective medication or gene therapy available for MSUD. The standard of care for MSUD requires lifelong compliance with an isoleucine, leucine, and valine restricted diet and the consumption of special medical foods/formulas prescribed by a licensed physician. This specialized medical nutrition management is medically supervised by a Geneticist and implemented by a registered dietitian specially trained in the nutrition management of inborn errors of metabolism. It requires frequent blood testing to control the blood levels of isoleucine, leucine, and valine, as well as close nutrition follow-up with the registered dietitian and medical team. The recommended treatment ranges of blood levels for individuals with MSUD are generally:

* Isoleucine: 50 – 150 μmol/L
* Leucine: 100-250 μmol/L
* Valine: 150-250 μmol/L

There is a strong correlation between cognitive function and maintenance of blood branched-chain amino acid levels in these treatment ranges. If dietary management is not sustained, neurological deterioration, phobias, difficulty in concentration and impulse control, and recurrent decompensation can occur. Currently, indefinite continuation of nutrition management is recommended for all patients with MSUD.

The specialized medical nutrition management for MSUD involves:

* A protein-restricted diet that excludes all foods high in protein (e.g. meat, poultry, fish, eggs, cheese, dairy, nuts, and legumes) and markedly restricts all grains, including rice, breads, and pastas
* Special low-protein modified food products (which are not available in grocery stores)
* Sufficient calorie intake that is evenly distributed throughout the day to prevent catabolism
* Prescribed amino acid-based medical foods/formulas that are free of isoleucine, leucine, and valine, the branched-chain amino acids to provide 80-85% of protein intake

The term medical food/formula, is defined in section 5(b) of the Orphan Drug Act {21 U.S.C. 360ee (b) (3)}: a “food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.”

Currently, this patient is prescribed **[CURRENT FORMULA PRODUCT],** which *is a/are* medical food/formula(s) used to manage MSUD. The amino acids in medical food/formula are the primary protein constituent (in general 80-85% of protein needs) for the MSUD dietary treatment regimen. Medical nutrition therapy must also provide a sufficient and balanced intake of other nutrients to avoid nutritional deficiencies. Nutrition therapy of MSUD without the use of medical foods is not possible, because it would cause severe protein malnutrition, calorie deprivation, vitamin and mineral deficiency, failure-to-thrive, and, ultimately, death.

**[CAMBROOKE PRODUCT NAME]** is only available by prescription through a pharmacy, durable medical equipment (DME) company, or directly from the manufacturer, Cambrooke Therapeutics, Inc. **[PATIENT NAME]** requires **[# OF GRAMS]** grams of protein equivalents per day from medical food/formula; therefore, we have prescribed **[AMOUNT OF PRODUCT]** per day to meet the protein requirements for MSUD.

We appreciate your attention to this request for **[CAMBROOKE PRODUCT NAME**] medical food/formula(s), **[AMOUNT OF PRODUCT]** to be covered by their current medical insurance.

Please do not hesitate to contact us if you have any questions.

Sincerely,

**[Physician name, M.D.]**

**[Physician’s credentials, contact info, clinic name]**

**[Dietitian name, RD, LDN]**

Cc: **[Parents’ names]**

**References:**

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6. Camp, K.M., Lloyd-Puryear, M.A., & Huntington, K.L. (2012). Nutritional treatment for inborn errors of metabolism: indications, regulations, and availability of medical foods and dietary supplements using phenylketonuria as an example. *Mol Genet Metab*. September; 107(1-2): 3–9.
7. Marriage, B. (2010). Chapter 6 Inherited disorders of branched-chain amino acid metabolism. In PB Acosta (Eds.), *Nutrition Management of Patients with Inherited Metabolic Disorders* (pp. 176-194). Sudbury, Massachusetts: Jones and Bartlett Publishers.