**LETTER OF MEDICAL NECESSITY: IVA**

**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 **Isovaleric Acidemia (IVA) (ICD 10: E71.110)** 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 IVA.

IVA results from a deficiency of the enzyme responsible for metabolizing the amino acid leucine. This deficiency results in the toxic build-up of organic acids in the body. Isovaleric Acidemia is part of the newborn screening profile due to the devastating effects if undiagnosed or untreated. The disorder occurs in both an acute and a chronic intermittent form. In the acute form of Isovaleric Acidemia, vomiting, refusal to eat, and listlessness usually occur and can be life-threatening. Elevated levels of leucine in patients with IVA can acutely lead to an encephalopathic crisis. Acute crisis is usually triggered by an illness and the frequency of crisis usually declines after the first few years of life. With treatment and low protein diet, the disorder becomes chronically intermittent, and a nearly normal life is possible.

The three primary goals of treatment are:

1. To maintain a blood level of leucine that is not toxic
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 IVA. The standard of care for IVA requires lifelong compliance with a very low protein, leucine restricted diet, supplementation with carnitine and glycine, as well as 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 leucine as well as close nutrition follow-up with the registered dietitian and medical team. The recommended treatment range of blood levels for individuals with IVA is generally:

* Leucine: 70-170 μmol/L

For patients with IVA there is a strong correlation between cognitive function and strict control of leucine. Long term problems in a patient with IVA that is chronically poorly managed can include poor growth, ataxia, learning problems, irreversible brain damage as well as severe and progressive neurological disorders. Neurological deterioration, lethargy, ataxia and coma can occur at any time if dietary management is not sustained. Currently, indefinite continuation of strict nutrition management is recommended for all patients with IVA.

The specialized medical nutrition management for IVA involves:

* A leucine-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 leucine to provide 60-65% of protein needs

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 **ISOVACTIN AA PLUS,** which is medical food/formula(s) used to manage IVA. The amino acids in medical food/formula are the primary protein constituent (in general 60-65% of protein needs) for the IVA dietary treatment regimen. Medical nutrition therapy must also provide a sufficient and balanced intake of calories and other nutrients to avoid fasting and nutritional deficiencies. Nutrition therapy of IVA 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.

**ISOVACTIN AA PLUS** 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 **[# of tetras]** drink cartons of **ISOVACTIN AA PLUS** per day (250 mL each) to meet the protein requirements for IVA.

We appreciate your attention to this request for **ISOVACTIN AA PLUS** 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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