

# Isovactin AA Plus 20 gram Protein Equivalent

## PRODUCT INFORMATION

Isovactin AA Plus 20 gram Protein Equivalent

250 mL carton (8.5 fl. oz) Reimbursement Code: 24359-0702-03

Manufactured by Cambrooke Therapeutics, Inc. Ayer, MA 01432 [www.cambrooke.com](http://www.cambrooke.com)

## DISPENSE BY PRESCRIPTION

Isovactin AA Plus is a leucine-free medical food for the dietary management of Isovaleric Acidemia (IVA).

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## DESCRIPTION

Isovactin AA Plus is a specially formulated ready to drink prescription medical food for the clinical dietary management of Isovaleric Acidemia (IVA) or isovaleryl-CoA dehydrogenase deficiency.

Isovactin AA Plus is to be used only under medical supervision. Isovactin AA Plus has been developed, labeled and should be administered in accordance with the Food and Drug Administration's (FDA's) regulatory definition of Medical Foods.

Congress defines "Medical Food" in the Orphan Drug Act and Amendments of 1988 as a formulation to be administered enterally (for oral or tube feeding) 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. 21 U.S.C. 360ee(b)(3).

Isovactin AA Plus is a ready-to-drink leucine-free medical food supplied in single dose, opaque 250 mL cartons, 30 cartons per case. Each carton contains 186 calories, 20 grams of protein equivalent per serving and a complete micronutrient profile.

## PRIMARY INGREDIENTS

Isovactin AA Plus is a leucine-free amino acid supplement that also contains carbohydrates, fats and a complete micronutrient profile. Isovactin AA Plus is indicated for those with Isovaleric Acidemia as those with this condition are unable to adequately breakdown leucine. Isovactin AA Plus is not intended as sole source nutrition and must be balanced with a tolerated leucine intake, typically from foods or intact protein source. It is generally recommended that a leucine-free supplement in conjunction with a low protein diet be continued as life-long treatment for optimal health.<sup>1</sup>

## Micronutrients and Macronutrients

Individuals with Isovaleric Acidemia should limit their intake of the essential amino acid leucine. Leucine is found naturally in nearly all protein-containing foods, including meats, dairy, legumes, grains, and, to a lesser degree, in vegetables and fruits. Such a severely restricted diet brings meaningful risk and challenges to receiving recommended daily intake of essential nutrients. To compensate for this, Isovactin AA Plus provides leucine-free protein equivalent to help provide essential and non-essential amino acids, adequate caloric intake with a balance of carbohydrate and fats and a complete micronutrient profile. Some amount of leucine is still essential, and is typically consumed with a low protein diet.

## Essential Fats

Isovactin AA Plus contains essential fatty acids in the amount of 1145 mg linoleic

acid and 549 mg linolenic acid. Isovactin AA Plus also contains 150 mg of the algae-sourced docosahexaenoic acid (DHA). Essential fatty acids cannot be produced in the body and therefore must be obtained through diet. Isovactin AA Plus contains essential fatty acids and DHA to help support brain and eye development.<sup>2</sup>

### **Digestive and Oral Health**

Isovactin AA Plus contains per serving 2 grams of inulin, a pre-biotic fiber which helps to support digestive health and enhance mineral absorption.<sup>3</sup>

Isovactin AA Plus provides a more neutral pH compared to other ready to drink amino acid based formulas. Ready to drink amino acid formulas typically have a low or acidic pH. With frequent consumption, this may lead to oral health problems. A pH less than 5.5 may lead to dental erosion.<sup>4</sup> Isovactin AA Plus has a pH of 5.8 making it gentler on digestion and tooth enamel.

### **Bone Health**

Isovactin AA Plus contains a bone health blend designed to optimize bone health. Bone health is a growing concern in individuals with inherited disorders of metabolism. Studies have found that 30-50% of those with phenylketonuria, a similar inherited disorder of metabolism, have a decreased bone mineral density<sup>5,6,7</sup> which may lead to osteoporosis and fractures if not detected and treated.<sup>6,7,8</sup> Isovactin AA Plus contains a unique blend of nutrients essential to bone health including 677 mg calcium, 620 IU vitamin D, 664 mg phosphorus, 5 mg zinc, and 143 mg magnesium per serving. In addition, Isovactin AA Plus contains 40 mcg of vitamin K per serving in the forms of both K1 and K2.

Vitamin K1 is activated to K2 in the body and plays a role as co-factor in the carboxylation of osteocalcin. Lower levels of carboxylated osteocalcin are associated with increased fracture risk.<sup>9</sup> In addition, Isovactin AA Plus contains 2 grams per serving of inulin, a soluble prebiotic fiber. Inulin consumed at 3 grams per day has been shown to aid in calcium absorption.<sup>3</sup>

### **Complete Ingredients**

Water, amino acid blend (L-alanine, glycine, L-proline, L-arginine, L-glutamine, L-lysine, L-tyrosine, L-phenylalanine, L-serine, L-carnitine, L-aspartic acid, L-threonine, L-valine, L-isoleucine, L-histidine, L-menthionine, L-tryptophan, L-cystine, taurine), vitamins and minerals (calcium lactate, monosodium phosphate, monopotassium phosphate, choline bitartrate, magnesium amino acid chelate, sodium ascorbate, ascorbic acid, dl-alpha-tocopheryl acetate, Fe amino acid chelate, niacinamide, zinc amino acid chelate, calcium d-pantothenate, manganese sulfate, riboflavin, B6 Pyridoxal 5' Phosphate, thiamin HCl, copper gluconate, L-methylfolate, vitamin A palmitate, potassium iodide, sodium selenite, cholecalciferol, K1 phytonadione, K2 MK-7, sodium molybdate, cholecalciferol, chromium chloride, biotin, B12 methylcobalamin), canola oil, sugar, natural flavors (propylene glycol, water, potassium sorbate), inulin, cellulose gel and carboxymethylcellulose sodium, food starch modified, sodium hexametaphosphate, DHA algal oil, acesulfame potassium, carrageenan, sucralose. Contains corn and soy.

### **INGREDIENT SAFETY**

The ingredients in Isovactin AA Plus are all approved food additives or Generally Recognized As Safe (GRAS) for the use in a medical food for individuals that have Isoleucic Acidemia. GRAS is the statutory safety standard of the U.S. Food and Drug Administration (FDA). The standard for an ingredient to achieve GRAS

status for a certain use requires technical demonstration of non-toxicity and safety, general recognition of safety through widespread usage and agreement by experts in the field.

## **MEDICAL FOOD STATUS**

### **INDICATIONS FOR USE**

Isovactin AA Plus is a ready to drink leucine-free medical food for the dietary management of individuals under a physician's care for Isovaleric Acidemia or other disorders involving leucine metabolism.

### **CLINICAL EXPERIENCE**

Individuals with isovaleric acedemia (IVA) are unable to adequately metabolize the essential amino acid, leucine. As a result, leucine and its by-products can accumulate in the blood. Protein naturally contains leucine, and as such, protein from the diet needs to be significantly reduced to ensure leucine consumption is limited. Protein, however, is essential for the body and is vital in the maintenance of body tissue, including development and repair. Even though individuals with Isovaleric Acidemia cannot have large amounts of leucine, they still require other amino acids to help maintain healthy muscle and tissue. The major source of dietary protein for those with an amino acid metabolism disorder consists of mixtures of synthetic amino acid formulas devoid of the offending amino acid(s) and a small amount of dietary protein mostly from fruits and vegetables or alternative intact protein source.<sup>1</sup> The use of synthetic amino acid formulas and a low protein diet are considered by many to be the standard of care for those with amino acid metabolism disorders.<sup>1</sup> Without control of leucine consumed, individuals with Isovaleric Acidemia can develop failure to gain weight, frequent vomiting, seizures, and delayed development.<sup>10</sup> Treatment with a low protein diet and appropriate medical food, such as Isovactin AA Plus, should be started as early as possible and be continued as life-long treatment.<sup>1,10</sup>

### **PHARMACOKINETICS**

Isovaleric Acidemia is caused by an absence or virtual absence of isovaleryl-CoA dehydrogenase (IVD) enzyme. IVD is necessary to break down leucine from food. In people without IVA, the IVD enzyme breaks down leucine. Those with IVA do not have enough of the IVD enzyme, which can cause feeding difficulties, vomiting, lethargy, and seizures. If these symptoms are not identified and treated quickly, Isovaleric Acidemia can lead to coma and death. With the use of a synthetic amino acid formula, patients are able to consume adequate protein equivalent with the remaining amino acids. Since the amino acids are already broken down to their simplest form, they may not be absorbed as efficiently as an intact protein. It is recommended that those with IVA consume 30-35% more protein than the Dietary Reference Intakes (DRIs).<sup>1</sup>

### **Precautions and Contraindications**

Isovactin AA Plus is intended to help meet nutritional requirements for patients 12 months and older with diagnosed Isovaleric Acidemia or other disorders involving leucine metabolism. It is not to be used as sole source nutrition. Individuals with other inborn errors of amino acid metabolism or those without a diagnosis of Isovaleric Acidemia can experience complications if using this product due to its lack of leucine which contributes to feeding difficulties, nausea, vomiting, lethargy, and hypotonia. Failure to consume some amount of the essential amino acid leucine can lead to death.<sup>1</sup>

Isovactin AA Plus contains corn and soy and is not suitable for individuals with an allergy to corn and/or soy.

### **Adverse Reactions**

Post – marketing surveillance has shown no adverse reactions.

### **Drug Interactions**

None known.

### **Toxicity**

None known.

### **SPECIAL POPULATIONS**

Indicated for Isovaleric Acidemia patients over 12 months of age. Always check with the monitoring physician for proper dosage recommendations.

Compliance to a low protein diet must accompany the use of Isovactin AA Plus for all Isovaleric Acidemia patients.

### **DOSAGE AND ADMINISTRATION**

Must be administered under physician supervision.

Recommended daily requirements vary with age, weight and activity levels. Follow recommendation of the medical practitioner to determine the amount of Isovactin AA Plus to be used each day.

### **HOW SUPPLIED**

Isovactin AA Plus provides 20 grams Protein Equivalent per serving and is supplied in 250 mL (8.5 fl. oz.) cartons.

The cartons are packaged 30 per case (reimbursement code: 24359-0702-03). Keep sealed in a cool, dry place. Refrigerate after opening. Do not freeze.

### **REFERENCES**

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