

Promactin AA Plus 20 gram Protein Equivalent

PRODUCT INFORMATION

Promactin AA Plus 20 gram Protein Equivalent

250 mL carton (8.5 fl. oz) Reimbursement Code: 24359-0703-03

Manufactured by Cambrooke Therapeutics, Inc. Ayer, MA 01432 www.cambrooke.com

DISPENSE BY PRESCRIPTION

Promactin AA Plus is a methionine, valine and threonine-free, low in isoleucine, medical food for the dietary management of propionic acidemia (PA) and methylmalonic acidemia (MMA).

DESCRIPTION

Promactin AA Plus is a specially formulated ready to drink prescription medical food for the clinical dietary management of propionic acidemia (PA) and methylmalonic acidemia (MMA.)

Promactin AA Plus is to be used only under medical supervision. Promactin 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).

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PRIMARY INGREDIENTS

Promactin AA Plus is a methionine, valine, threonine-free, low in isoleucine, amino acid supplement that also contains carbohydrates, fats and a complete micronutrient profile. Promactin AA Plus is indicated for those with propionic acidemia and methylmalonic acidemia. Promactin AA Plus is not intended as a sole source of nutrition and must be balanced with a tolerated methionine, valine, threonine and isoleucine intake, typically from foods or intact protein source. It is generally recommended that an amino acid supplement free or low in propiogenic amino acids in conjunction with a low protein diet be continued as life-long treatment for optimal health.¹

Micronutrients and Macronutrients

Individuals with propionic or methylmalonic acidemia should limit their intake of propiogenic amino acids including methionine, valine, threonine and isoleucine. These amino acids are found naturally in nearly all protein containing foods, including meats, dairy, legumes, grains, and to a lesser degree, 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, Promactin AA Plus provides methionine, valine, and threonine-free, low in isoleucine, 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 methionine, valine, threonine and isoleucine is still essential and is typically consumed with a low protein diet.

Essential Fats

Promactin AA Plus contains essential fatty acids in the amount of 1145 mg linoleic acid and 549 mg linolenic acid. Promactin AA Plus also contains 150 mg of algae-sourced docosahexaenoic acid (DHA). Essential fatty acids cannot be produced in the body and therefore must be obtained through diet. Promactin AA Plus contains essential fatty acids and DHA to help support brain and eye development.²

Digestive and Oral Health

Promactin AA Plus provides a more neutral pH compared to other ready to drink amino acid based formulas. Ready to drink amino acid based 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.³ Promactin AA Plus has a pH of 5.8 making it gentler on digestion and tooth enamel.

Bone Health

Promactin 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. Those with propionic or methylmalonic acidemia have increased risk of osteopenia and osteoporosis likely related to a variety of factors including protein deficiency, chronic metabolic acidosis, micronutrient deficiency and reduced weight bearing exercise.¹

Promactin 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, Promactin 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.⁴

Complete Ingredients

Water, amino acid blend (L-leucine, L-aspartic, L-lysine HCl, L-alanine, L-arginine, L-serine, L-histidine, L-tyrosine, L-phenylalanine, L-glutamine, L-proline, L-glycine, L-cystine, L-tryptophan, L-isoleucine, taurine, L-carnitine, maltodextrin), 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 pantothenate, manganese sulfate, riboflavin, B6 pyridoxine HCl, thiamin HCl, copper gluconate, folic acid, vitamin A palmitate, potassium iodide, sodium selenite, cholecalciferol, K1 phytonadione, K2 MK-7, sodium molybdate, cholecalciferol, chromium chloride, biotin, B12 cyanocobalamin), canola oil, sugar, natural flavors (propylene glycol, water, potassium sorbate), 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 Promactin AA Plus are all approved food additives or Generally Recognized As Safe (GRAS). 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

Promactin AA Plus is a ready to drink methionine, valine, and threonine-free, low in isoleucine, medical food for the dietary management of individuals under a physician's care for propionic acidemia (PA) or methylmalonic acidemia (MMA.)

CLINICAL EXPERIENCE

Individuals with propionic or methylmalonic acidemia are unable to adequately metabolize the essential amino acids, methionine, valine, threonine and isoleucine, as well as odd-chain fatty acids. Some individuals with propionic acidemia may respond to enzyme co-factor vitamin B6. Some individuals with methylmalonic acidemia may respond to enzyme co-factor related vitamin B12. Residual enzyme activity determines the degree of dietary restriction required.^{1,5} Avoidance of fasting is important to prevent the breakdown of body fat stores, which include odd-chain fatty acids.¹ Proteins naturally contains methionine, valine, threonine, and as such, protein from the diet needs to be significantly reduced to ensure the consumption of these amino acids is limited. Protein is essential for the body and is vital in the maintenance of body, including tissue synthesis and repair. Even though those with propionic or methylmalonic acidemia cannot have large amounts of methionine, valine threonine and isoleucine, they do 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.⁵ The use of synthetic amino acid formulas and low protein diet is often considered the standard of care for those with amino acid metabolism disorders.¹ Without control of the amount of methionine, valine, threonine and isoleucine consumed, individuals with propionic acidemia and methylmalonic acidemia can develop significant impairments including metabolic crisis, failure to thrive, anorexia, movement disorders, developmental delay, seizures and chronic kidney failure.⁵ Initial treatment of a low protein diet and appropriate medical food, such as Promactin AA Plus, should be started as early as possible and treatment should be continued throughout life.^{1,5}

PHARMACOKINETICS

Propionic acidemia and methylmalonic acidemia are typically caused by a deficiency in the enzymes propionyl-CoA carboxylase (PCC) and methylmalonyl-CoA mutase (MMM), respectively. These enzymes are involved in the pathway which processes methionine, valine, threonine and isoleucine, as well as odd chain fatty acids. In people without these disorders, the PCC and MMM enzymes help to process excess methionine, valine, threonine and isoleucine. Those with propionic and methylmalonic acidemias do not have enough of the either PCC or MMM enzymes, which can cause an accumulation of toxic organic compounds.^{1,5} Chronic build-up of these compounds can lead to problems such as metabolic crisis, failure to thrive, anorexia, movement disorders, developmental delay, seizures and chronic kidney failure.⁵ With the use of a synthetic amino acid formula, patients are able to consume adequate protein equivalent with the remaining amino acids and receive a balance of other important macro and micronutrients.^{1,5} Since amino acids are already broken down to their simplest form, they may not be absorbed as efficiently as intact protein. It is recommended that those taking protein equivalent as amino acids consume 30-35% more protein than the Dietary Reference Intakes (DRIs.)¹

Precautions and Contraindications

Promactin AA Plus is intended to help meet nutritional requirements for patients 12 months and older with diagnosed propionic or methylmalonic acidemia. It is not to be used as sole source nutrition. Individuals with other inborn errors of amino acid metabolism or those without a propionic or methylmalonic acidemia diagnosis can experience complications if using this product due to its lack of methionine, valine, threonine and isoleucine. Failure to consume essential amino acids, which are those amino acids unable to be produced by the body, can lead to growth failure and even death.^{1,5}

Promactin 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 those with propionic or methylmalonic acidemia 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 Promactin AA Plus for all propionic acidemia and methylmalonic acidemia patients, including those considering having children or who are pregnant.

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 Promactin AA Plus to be used each day.

HOW SUPPLIED

Promactin 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: 24359-0703-03). Keep sealed in a cool, dry place. Refrigerate after opening. Do not freeze.

REFERENCES

- 1 Nutrition Management of Patients with Inherited Metabolic Disorders. Acosta PB, editor. Jones and Bartlett Publishers, Sudbury, MA. 2010.
- 2 Singh M. Essential fatty acids, DHA and human brain. Indian J Pediatr. 2005 Mar;72(3):239-42.
- 3 Touger-Decker, R., van Loveren, C. Sugars and dental caries. The American Journal of Clinical Nutrition. 78, 8815-8925.
- 4 Marieke, J. et al. (2008). Vitamin K status is associated with childhood bone mineral content. British Journal of Nutrition, 100, 852-858.
- 5 Boyer SW, Barclay LJ, Burrage LC. Inherited Metabolic Disorders: Aspects of Chronic Nutrition Management. Nutr Clin Pract. 2015 Aug;30(4):502-10.