

Homactin AA Plus 20 gram Protein Equivalent

PRODUCT INFORMATION

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250 mL carton (8.5 fl. oz) Reimbursement Code: 24359-0701-03

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

DISPENSE BY PRESCRIPTION

Homactin AA Plus is a methionine-free medical food for the dietary management of homocystinuria (HCU).

DESCRIPTION

Homactin AA Plus is a specially formulated ready to drink prescription medical food for the clinical dietary management of homocystinuria (HCU.)

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

Homactin AA Plus is a ready-to-drink methionine-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

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

Micronutrients and Macronutrients

Individuals with homocystinuria should limit their intake of the essential amino acid methionine. Methionine is 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, Homactin AA Plus provides methionine-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 methionine is still essential and is typically consumed with a low protein diet.

Essential Fats

Homactin AA Plus contains essential fatty acids in the amount of 1145 mg linoleic acid and 549 mg linolenic acid. Homactin 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. Homactin AA Plus contains essential fatty acids and DHA to help support brain and eye development.²

Digestive and Oral Health

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

Homactin 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.⁴ Homactin AA Plus has a pH of 5.8 making it gentler on digestion and tooth enamel.

Bone Health

Homactin 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. Individuals with homocystinuria have a significantly greater risk of skeletal abnormalities, osteoporosis, scoliosis and fracture.⁵ Homocysteine and its impact on collagen formation in bone may be the reason for skeletal defects.⁶

Homactin 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, Homactin 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.⁷ In addition, Homactin 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.³

Complete Ingredients

Water, amino acid blend (L-leucine, L-aspartic, L-proline, L-lysine HCl, L-valine, L-arginine, glycine, L-isoleucine, L-tyrosine, L-glutamine, L-serine, L-threonine, L-phenylalanine, L-alanine, L-histidine, L-cystine, L-tryptophan, taurine, L-carnitine, maltodextrin), vitamins and minerals (calcium lactate, monosodium phosphate, monopotassium phosphate, choline bitartrate, magnesium amino acid chelate, sodium ascorbate, ascorbic acid, dlalpha-tocopheryl acetate, Fe amino acid chelate, niacinamide, zinc amino acid chelate, calcium d-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), 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 Homactin AA Plus are all approved food additives or Generally Recognized As Safe (GRAS) for the use in a medical food for individuals that have homocystinuria. 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

Homactin AA Plus is a ready to drink methionine-free medical food for the dietary management of individuals under a physician's care for homocystinuria (HCU.)

CLINICAL EXPERIENCE

Individuals with homocystinuria (HCU) are unable to adequately metabolize the essential amino acid, methionine. As a result, homocysteine, a methionine by-product, can accumulate to toxic levels in the blood. Complications can include problems with the eyes, abnormal blood clotting, skeletal abnormalities and intellectual disability.⁵ Approximately half of those with homocystinuria may respond to high doses of enzyme co-factor vitamin B6 and the remainder must follow a low-methionine diet.⁵ Methionine is found naturally in protein, and as such, protein from the diet needs to be significantly reduced to ensure methionine consumption is limited. Protein, however, is essential for the body and is vital in the maintenance of the body, including tissue synthesis and repair. Even though those with homocystinuria cannot have large amounts of methionine, 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.⁸ The use of synthetic amino acid formulas and low protein diet is the standard of care for those with amino acid metabolism disorders.⁵ Without control of the amount of methionine consumed, individuals with homocystinuria who do not respond to B6 supplementation can develop significant impairments including damage to the retina, cardiovascular health and intellectual development.⁵ Initial treatment of a low protein diet and appropriate medical food, such as Homactin AA Plus, should be started as early as possible and treatment should be continued throughout life.^{1,5}

PHARMACOKINETICS

Homocystinuria is typically caused by a deficiency in the enzyme cystathionine beta synthase (CBS,) though other enzymatic defects do exist that can also result in classical homocystinuria. CBS is necessary to break down excess methionine not needed for body protein synthesis. In people without HCU, the CBS enzyme processes excess methionine. Those with HCU do not have enough of the CBS enzyme, which can cause methionine, and related by-product homocysteine, to build up in the blood and brain to toxic levels. Additionally, cysteine levels may become deficient and become conditionally essential in those with homocystinuria. Chronically elevated levels of homocystine likely causes the complications associated with HCU including eye problems, blood clots and developmental delay. With the use of a synthetic amino acid formula, patients are able to consume adequate protein equivalent with the remaining amino acids. 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

Homactin AA Plus is intended to help meet nutritional requirements for patients 12 months and older with diagnosed homocystinuria. It is not to be used as sole

source nutrition. Individuals with other inborn errors of amino acid metabolism or those without a homocystinuria diagnosis can experience complications if using this product due to its lack of methionine which contributes to mood regulation, alertness, dopamine transmission, learning and memory. Failure to consume essential amino acids, those unable to be produced by the body, can lead to growth failure and even death.^{5,8}

Homactin 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 homocystinuria patients over 12 months of age. Always check with the monitoring physician for proper dosage recommendations.

Compliance to a low methionine diet must accompany the use of Homactin AA Plus for all homocystinuria 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 Homactin AA Plus to be used each day.

HOW SUPPLIED

Homactin 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: 24359-0701-03). Keep sealed in a cool, dry place. Refrigerate after opening. Do not freeze.

REFERENCES

- 1 Picker JD, Levy HL. Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency. 2004 Jan 15 [Updated 2014 Nov 13]. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK1524/>.
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- 6 Lim JS, Lee DH. Changes in bone mineral density and body composition of children with well-controlled homocystinuria caused by CBS deficiency. *Osteoporos Int.* 2013 Sep;24(9):2535-8.
- 7 Marieke, J. et al. (2008). Vitamin K status is associated with childhood bone mineral content. *British Journal of Nutrition,* 100, 852-858.
- 8 Boyer SW, Barclay LJ, Burrage LC. Inherited Metabolic Disorders: Aspects of Chronic Nutrition Management. *Nutr Clin Pract.* 2015 Aug;30(4):502-10.