Tylactin BUILD™ 20 gram Protein Equivalent
(modified glycomacropeptide for tyrosinemia)

PRODUCT INFORMATION
Tylactin BUILD 20 gram Protein Equivalent
(modified glycomacropeptide for tyrosinemia)
28 g packet (1 oz) Reimbursement Code: 24359-0541-07
Manufactured by Cambrooke Therapeutics, Inc. Ayer, MA 01432 www.cambrooke.com

DISPENSE BY PRESCRIPTION
Tylactin BUILD (modified glycomacropeptide for tyrosinemia) is a medical food for the dietary management of tyrosinemia (TYR).

DESCRIPTION
Tylactin BUILD (modified glycomacropeptide for tyrosinemia) is a specially formulated prescription medical food for the clinical dietary management of Hereditary Furmarylacetoacetase Deficiency (Tyrosinemia Type I), Oculocutaneous Tyrosinemia (Tyrosinemia Type II), and Type III.

Tylactin BUILD is to be used only under medical supervision. Tylactin BUILD has been developed, labeled and should be administered in accordance with the FDA statutory and 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 (or orally) 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.

Tylactin BUILD is a powder medical food to be reconstitution with a liquid of choice, supplied in 20g protein equivalent pouch, thirty pouches per case. Tylactin BUILD comes with a complete micronutrient and macronutrient profile. Tylactin BUILD contains a small amount of tyrosine and phenylalanine: 3 mg tyrosine, 8 mg phenylalanine per 1 oz (28g) pkt.

PRIMARY INGREDIENTS
Glycomacropeptide
Glycomacropeptide (GMP) is a 64-amino acid whole protein derived from whey. GMP has a unique amino acid profile, which includes an absence of the aromatic amino acids, phenylalanine, tryptophan and tyrosine and higher concentrations of isoleucine and threonine, compared to other dietary proteins. The naturally low levels of tyrosine and phenylalanine contained in commercial GMP make this protein an alternative to synthetic free amino acid based protein for the management of TYR. The GMP in Tylactin BUILD is modified by enhancing levels of tryptophan, arginine, leucine, histidine, and cysteine which are naturally deficient in pure GMP. The addition of these amino acids is necessary to meet daily-required intake of these essential and indispensable amino acids, which cannot be synthesized de novo by the body. While GMP in its pure form contains no tyrosine or phenylalanine, the process of extracting and refining glycomacropeptide results in the inclusion of trace quantities of tyrosine and phenylalanine (about 0.02 mg of tyrosine and 1.8 mg of phenylalanine per protein equivalent gram). Tyrosine and phenylalanine are the offending amino acids in Tyrosinemia Type I, II, and III and intake must be severely restricted to prevent neurodevelopmental and physiological consequences.

Micronutrients and Macronutrients
Patients with Tyrosinemia have a severely restricted diet to minimize intake of amino acids phenylalanine and tyrosine that are found naturally in all foods containing protein, including all meats, dairy, legumes, and many vegetables, fruits and grains. Tyrosine is low in natural protein but phenylalanine is a precursor of tyrosine, so limiting phenylalanine intake limits the phenylalanine-tyrosine conversion. As such, there is meaningful risk and challenges in receiving recommended daily intake of many micronutrients. To compensate for this, Tylactin BUILD includes a full profile of micronutrients and macronutrients.
**Complete Ingredients**

Glycomacropeptide, L-leucine, sunflower oil, L-arginine, inulin, glycine, maltodextrin, vitamin and mineral blend (retinyl palmitate, ascorbic acid, cholecalciferol, dl-tocopherol acetate, phylloquinone, menaquione, thiamine mononitrate, riboflavin, niacinamide, pyridoxine hydrochloride, folic acid, cyanocobalamin, calcium pantothenate, choline bitartrate, D-biotin, potassium lactate, chromium chloride, copper gluconate, ferrous fumarate, magnesium phosphate, manganese sulfate, sodium molybdate, magnesium phosphate, potassium phosphate, sodium selenite, zinc sulfate, potassium chloride), L-lysine acid, L-histidine, L-tryptophan, natural flavor, Bacillus coagulans GBI-30 6086. Contains milk.

**GENERALLY RECOGNIZED AS SAFE**

The ingredients in Tylactin BUILD are Generally Recognized As Safe (GRAS). This is the statutory safety standard of the U.S. Food and Drug Administration (FDA). The standard for an ingredient to achieve GRAS status 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**

Tylactin BUILD is a medical food for the dietary management of individuals under a physician’s care for Hereditary Fumarylacetoacetase Deficiency (Tyrosinemia Type I), Oculocutaneous Tyrosinemia (Tyrosinemia Type II), and Type III.

**TYROSINEMIA, PHENYLALANINE AND PHENYLKETONURIA (PKU)**

Tyrosinemia patients have a defective enzyme fumarylacetoacetate which affects the conversion of tyrosine to neurotransmitters and metabolites. Tyrosine is present in very low levels in natural dietary protein but is biosynthesized within the body based on the level of consumption of phenylalanine. Blood levels and dietary monitoring must be done for both phenylalanine and tyrosine. Tyrosinemia is similar to phenylketonuria (PKU) which involves an enzyme defect in the same phenylalanine-tyrosine pathway. (PKU patients have a defect in the enzyme phenylalanine hydroxylase which affects the conversion of phenylalanine to tyrosine.) Both disorders require lifelong dietary protein intake based on the levels of phenylalanine that are consumed.

**CLINICAL EXPERIENCE**

Inpatient clinical studies completed at the University of Wisconsin with eleven phenylketonuria patients were conducted to investigate the safety and acceptability of substituting protein from glycomacropeptide for synthetic amino acid formula. Subjects consumed their usual amino acid diet when measured 2.5 hours after consumption. GMP compared with the synthetic amino acid diet showed a significant increase in urea production and instead are retained for protein synthesis compared with synthetic amino acid diets. This result is consistent with slower absorption of amino acids from an intact natural source of protein. It also suggests that fewer amino acids are degraded for urea production and instead are retained for protein synthesis when glycomacropeptide is substituted for synthetic amino acids as a protein source.

**Pharmacokinetics**

Tylactin (modified glycomacropeptide for tyrosinemia) contains glycomacropeptide as a primary ingredient. The low level of aromatic amino acids (phenylalanine, tryptophan and tyrosine), and concentration of large neutral amino acids (LNAs) threonine, valine and isoleucine make glycomacropeptide an ideal protein replacement therapy for tyrosinemia patients. The natural high concentration of LNAs in glycomacropeptide are enhanced with supplemental LNAs to compete with the offending amino acids tyrosine and phenylalanine for specific carrier proteins that transport LNAs across the intestinal mucosa and blood-brain barrier. This increased competition likely restricts the ability of tyrosine and phenylalanine to enter the brain where it can become a neurotoxin leading to mental impairment for the patient with tyrosinemia.

**Precautions and Contraindications**

Tylactin BUILD is intended for the complete protein and micronutrient needs for patients with diagnosed tyrosinemia. Individuals with other inborn errors of protein metabolism or those without a tyrosinemia diagnosis can experience complications if using this product due to its extremely low level of tyrosine and phenylalanine which contribute to mood regulation, alertness, dopamine transmission, learning and memory.

**Adverse Reactions**

Post – marketing surveillance has shown no adverse reactions.

This figure shows the concentration of total amino acids in plasma was significantly greater, and the concentration of BUN was significantly lower, with Glycomacropeptide compared with the synthetic amino acid diet when measured 2.5 hours after consumption. This result is consistent with slower absorption of amino acids from an intact natural source of protein. It also suggests that fewer amino acids are degraded for urea production and instead are retained for protein synthesis when glycomacropeptide is substituted for synthetic amino acids as a protein source.

**Pharmacokinetics**

Tylactin BUILD contains protein from whey. Therefore, it may not be suitable for those with an allergy to milk or milk products.

**Tylactin BUILD**

Tylactin BUILD contains a small amount of tyrosine and phenylalanine (0.15 mg of tyrosine and 4 mg of phenylalanine per protein equivalent gram) due to the process of extracting and refining glycomacropeptide; the tyrosine and phenylalanine content needs to be accounted for in the total daily tyrosine and phenylalanine prescription.

**Post – marketing surveillance has shown no adverse reactions.**
Drug Interactions
None known.

Toxicity
None known.

SPECIAL POPULATIONS
• Approved for tyrosinemia patients over 12 months of age. Always check with physician for proper dosage recommendations.
• Tylactin BUILD has not sought FDA approval for use in infants with tyrosinemia, but glycomacropeptide is widely found in infant formula containing whey protein.
• Compliance to a low tyrosine/phenylalanine diet must accompany the use of Tylactin for all tyrosinemia patients, including those considering having children or who are pregnant.

DOSEAGE AND ADMINISTRATION
Must be administered under physician supervision. Add powder from one pouch to 6-12 oz (180-360 mL) of beverage or formula, or add to food. Mix well.
Recommended daily requirements vary with age, weight and activity levels. Follow recommendation of medical practitioner to determine the best amount of Tylactin BUILD to be used each day.

HOW SUPPLIED
Tylactin BUILD 20g Protein Equivalent is supplied in 1 oz (28 g) pkt pouches. The pouches are packaged 30 per case (reimbursement code: 24359-0541-07). Store in a cool, dry place.

REFERENCES
3 Burton-Freeman BM. Physiol Behav. 2008 Jan 28;93(1-2):379-87. Epub 2007 Oct 26. Glycomacropeptide is not critical to whey-induced satiety, but may have a unique role in energy intake regulation through cholecystokinin (CCK).