

## MEDICAL FOODS FOR THE NUTRITIONAL SUPPORT OF CHILD/ADULT METABOLIC DISEASES

### TECHNICAL FIELD

The present invention relates generally to a novel generic powder base rich in fats, carbohydrates, vitamins, minerals and trace elements which can be readily admixed with specific amino acids to yield several different therapeutic products for use in nutritional support of various inherited metabolic diseases.

### BACKGROUND OF THE INVENTION

The present invention relates to novel nutritional products (medical foods) for the treatment of various inherited metabolic disorders and methods of manufacturing these medical foods. These products comprise different amino acid mixtures in combination and admixture with a common nutritional base of fats, carbohydrates, vitamins and minerals (hereinafter referred to as the "Premix Base") which supplies the specific nutritional and energy requirements of the patient. Each individual amino acid formulation is particular for the nutritional support of a specific metabolic disorder as discussed below.

Inborn errors of metabolism occur when there is a block in a pathway in a metabolic sequence. The block results in an accumulation of normal intermediary products in abnormally large amounts and also of products of usually little used metabolic pathways. In most instances this effect can be attributed to the accumulation of an intermediary product proximal to the block. The accumulated toxic effects of these intermediary metabolites can be treated by restricting the intake of the essential substance from which the toxic metabolite is derived. Sometimes, the block prevents the synthesis of an essential compound normally made distal to the block and therapy consists of specifically providing this metabolite.

Infants with certain inborn errors of amino acid or nitrogen metabolism can be treated with special diets that restrict one or more amino acids to the minimum amount essential for normal growth. The amount of the restricted amino acid provided by the diet must be sufficient to meet the metabolic requirements dependent on it, but it must not permit an excess accumulation in the body fluids of the amino acid or its derivatives, or of nitrogen.

The nutrient requirements can be met by providing a semisynthetic diet, derived either from a modified protein hydrolysate or from a mixture of L-amino acids devoid of, or low in, the offending amino acid(s). Other food sources in prescribed amounts furnish the implicated amino acid(s) in an amount sufficient to support normal growth, yet low enough to avoid toxicity. Requirements for other essential nutrients are met by the addition of minerals and vitamins to the specific amino acid mixture during manufacture.

Careful monitoring is essential during nutritional support. The total nutrient intake should be known and monitored to be certain that the person is receiving a nutritionally adequate diet both in terms of essential nutrients as well as total energy intake. The plasma concentration of the appropriate amino acid(s) or ammonia in disorders of the urea cycle should be determined frequently to assure that the level is adequate to

sustain normal protein metabolism, but not high enough to be harmful.

Nutritionally balanced medical foods presently available provide adequate fat and carbohydrate, as well as essential protein, vitamins, and minerals. The total nutrient composition of the special dietary product is considered so that the product provides not only all of the amino acid requirements, except the implicated amino acids, but also trace minerals, vitamins, and other micronutrient requirements. For an infant, the special diet often also meets total energy needs. The requirement for the implicated amino acid may be derived from the addition of infant formula, or other selected foods in prescribed amounts. Conventional low protein foods are used as part of the diet for children after infancy.

Different types of products have been developed for use in diets of infants and of older persons with inborn errors of metabolism. Energy supplements can be combined with the appropriate amino acid mixtures, and limited conventional foods, for nutritional support under medical supervision.

For disorders of amino acid metabolism, products with specially treated protein hydrolysates or amino acid mixtures are used. All currently available commercial products require the addition of prescribed amounts of regular infant formula, milk, low protein or conventional foods.

From a historical perspective, essentially four types of medical foods are known. These may be summarized as follows:

Type 1 products contain levels of amino acids or protein, vitamins, and minerals appropriate for feeding infants with the exception of the amino acid(s) not metabolized by the patient.

Type 2 products contain somewhat higher levels of amino acids or protein, vitamins, and minerals to meet the needs of older subjects. However these products are all either devoid of or low in the amino acid(s) that cannot be metabolized by the patient.

Type 3 products include amino acid mixtures free of the amino acids which cannot be metabolized with complete vitamin and mineral supplements but with little or no added carbohydrate or fat.

Type 4 products consist of modules that require the addition of a special amino acid mixture for amino acid disorders, selected carbohydrates for disorders of carbohydrate metabolism or intolerance, or selected fat for disorders of fat metabolism or intolerance.

Whichever metabolic food is selected, it is done so with consideration for the patient's nutrient and energy needs. A person's actual dietary intake, growth and nutritional status, blood values for the implicated amino acid, and other tests for nutritional sufficiency are monitored periodically. Caution is needed when using special medical foods to treat disorders of amino acid metabolism because of the genetic individuality and particular nutrient needs of each patient. The preparation of specific diets from synthetic or semisynthetic products in combination with natural foods is best done by experienced people.

For older infants and children, in order to meet the total nutrient requirement, larger amounts of Type 1 medical foods must be consumed. This volume requirement may not allow sufficient flexibility in adding other foods to the diet. In such instances, Type 2 medical foods that are higher in protein, vitamins, and minerals, or Type 3 amino acid mixtures are then useful, since