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MEDICAL NUTRITION FOR INHERITED METABOLIC DISEASE
Corporate Medical Policy

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Document Precedence

BCBSVT Medical Policies are developed to provide clinical guidance and are based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. The applicable group/individual contract and member certificate language determines benefits that are in effect at the time of service. Since medical practices and knowledge are constantly evolving, BCBSVT reserves the right to review and revise its medical policies periodically. To the extent that there may be any conflict between medical policy and contract language, the member's contract language takes precedence.

Medical Policy

Description

Inherited metabolic disease is defined as a disease caused by an inherited abnormality of body chemistry for which the state screens newborn infants.

Over 700 inborn errors of metabolism (IEM) are known; they are hereditary defects that interfere with one or more biochemical functions that are essential for life. Disorders in the intermediary metabolism of protein, carbohydrate or lipids cause serious problems in infants and are most amenable to treatment with medical foods. In these disorders, either excess of one or more metabolites, or, conversely lack thereof from failure of endogenous synthesis, becomes critical and without correction of the metabolic abnormalities, severe systemic disease ensues. Although some IEM disorders require medical foods for treatment, many do not.

Definitions

Low protein modified food products are specifically formulated to have less than 1 gram of protein per serving and is intended to be used under the direction of a physician for the dietary treatment of a metabolic disease.

Medical foods are different from the broader category of foods in that they are an amino acid modified preparation, specially formulated and processed. They are intended for use under medical supervision to meet distinctive nutritional requirements of an inherited metabolic disease or condition.

An **inherited metabolic disease** is caused by a genetic defect which leads to life threatening abnormalities in body chemistry. Certain metabolic enzymes may be absent in individuals, and as a result, products of digestion which are normally further metabolized may accumulate in toxic amounts. Examples of these disorders include, but are not limited to phenylketonuria, hyperphenylalaninemia, maple syrup urine disease (ketoaciduria), histidinemia, homocystinuria, organic acidemias, tyrosinemia, and urea cycle disorders (citrullinemia, arginosuccinic aciduria). The rationale behind the use of "medical" foods is that the elements normally found in food which lead to the accumulation of these products of digestion are eliminated, so the toxic accumulation of by-products does not occur.

Medical foods are intended for the dietary treatment of a disease or condition for which nutritional requirements are established as medically necessary, and are formulated to be consumed or administered under the direction of a physician. Some types of medical foods may include:

A. Specially manufactured infant feeding formulas that have been developed to treat inborn errors of metabolism. Certain formulas eliminate the amino acid that cannot be metabolized. Oral nutrition formula for supplementation or dietary replacement is considered medically necessary for the treatment of inborn errors of metabolism, when the formula is required to prevent significant illness resulting from a byproduct in the metabolic pathway or amino acid accumulation, or to restore an essential nutrient that is lacking as a result of an inborn error of metabolism. See BCBSVT Medical Policy on Enteral Nutrition for more information.
B. Other medical foods for use by older children and adults are products that resemble natural food, but which have been either chemically synthesized or processed from natural food. These products are generally not available in supermarkets or grocery stores, but are obtained directly by mail order from the manufacturer. *Low protein modified food products* include special breads, pastas, baked goods, flour mixes, cheeses and broths which have been formulated to have less

than one gram of protein per serving and do not include natural foods that are naturally low in protein.

Policy Guidelines

Medical foods are considered **medically necessary** for the dietary treatment of inherited metabolic disease when prescribed by a physician and administered under the direction of a physician and meet ALL of the following criteria:

a) The product is being used to treat IMD/ IEM.
b) Use of product is essential for the treatment of IMD/IEM and failure to use medical foods will predictably result in adverse medical outcomes.
c) The product is labeled for the dietary mgmt of IMD/ IEM.
d) The product is labeled to be used under medical supervision.

The Plan covers formulas for enteral nutrition including low protein formula in accordance with Vermont State Mandate [i] for the medically necessary treatment of certain inherited metabolic diseases and inborn errors of metabolism (IEM), when prescribed by a physician. Please see BCBSVT medical policy on Enteral Nutrition for additional information.

As of the original effective date of this medical policy, the State of Vermont requires newborn screenings for the following metabolic disorders. Therefore medical foods and formulas prescribed for these disorders must be covered, subject to the benefit limitations described in this medical policy. This list is subject to change.

NOTE: *Not all listed conditions require medical foods or formulas.

- Argininosuccinic acidemia (ASA)[1] (270.6, E72.21)[2],
- Beta-ketothiolase deficiency (BKT) (270.3; E71.19),
- *Biotinidase Deficiency (277.6,D81.810),
- *Carnitine uptake defect (CUD) (277.81,E71.41),
- Citrullinemia (CIT) (270.6, E72.23),
- *Congenital adrenal hyperplasia (CAH) (255.2,E25.0),
- *Congenital Hypothyroidism (CH) (243,E03.1),
- *Cystic fibrosis (CF) (277.00,E84.9),
- Galactosemia (GALT) (271.1,E74.21),
- 3-OH 3-CH3 glutaric aciduria (HMG) (270.7,E71.118),
- Glutaric acidemia type I (GA I) (270.7,E72.3),
- *Hb S/Beta-thalassemia (Hb S/BTh) (282.41,D57.40),
- *Hb S/C disease (Hb S/C) (282.63,D57.20),
- Homocystinuria (HCY) (270.4,E72.11),

- Isovaleric acidemia (IVA) (270.3, E71.110),
- *Long-chain L-3-OH acyl-CoA dehydrogenase deficiency (LCHAD) (277.85,E71.318),
- Maple Syrup Urine Disease (MSUD) (270.3,E71.0),
- *Medium-chain acyl-CoA dehydrogenase deficiency (MCAD) (277.85,E71.311),
- 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC) (270.3,E71.19),
- Methylmalonic acidemia (Cbl A, B) (270.3,E71.120),
- Methylmalonic acidemia (mutase deficiency) (MUT) (270.3,E71.120),
- Multiple carboxylase deficiency (MCD) (270.3,D81.818),
- Phenylketonuria (PKU)(270.1,E70.0),
- Propionic acidemia (PROP)(270.3,E71.121),
- *Sickle cell anemia (Hb SS disease) (SS) (282.60,D57.1),
- *Trifunctional protein deficiency (TFP) (277.85,E71.318),
- Tyrosinemia type I (TYR I) (270.2,E70.21),
- *Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD) (277.85,E71.310)

[1]Condition Name and Abbreviation — curated by the NLM and selected from among the names used by the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC), National Newborn Screening Information System (NNSIS), the American College of Medical Genetics (ACMG), the HHS Office of the National Coordinator for Health Information Technology (ONC)/American Health Information Community (AHIC) Personalized Health Care Work Group, and input from the newborn screening community. [2] (ICD-9 code, ICD-10 Code).

Medical foods may be purchased from a durable medical equipment vendor, or ordered through the pharmacy or ordered directly from the manufacturer and shipped directly to the patient. Examples of some manufacturers/distributors of medical foods include:

1. Mead Johnson Nutrition
2. Abbott Nutrition
3. Vitaflo (Nestle Nutrition)
4. Applied Nutrition
5. Nutricia, N.A.
6. CamBrooke Foods, LLC.
7. Med-Diet, Inc.
8. Dietary Specialties, Inc.
9. Nestle, Inc.

Medical foods are not generally available in grocery stores, supermarkets, health food stores or over the counter at a retail pharmacy.

Exclusion/ Not Covered

We provide no Benefits for:

- Conventional food items. These are considered grocery items.
- Food supplements (e.g., Ensure, Sustacal) are not considered medical foods as they are generally available over-the-counter and are not formulated for the treatment of inherited metabolic disorders.
- Convenience items such as recipe books.
- Shipping and handling fees or costs.

Over-the-counter enteral nutrition is an exclusion from the member contracts.

BCBSVT does not provide coverage for nutritional formulae and supplements, this includes over-the-counter formulas or nutritional supplements and formulas that can be purchased in a supermarket, health food store, over-the-counter at a retail pharmacy (Ensure®, Similac®, Enfamil® [not an exhaustive list]) regardless of the route of administration and regardless of whether or not prescribed by a physician. Formulas and supplements described by HCPCS codes B4102-B4104; B4149-B4152 are in this category and are not covered.

Legislative Guidelines

This policy complies with Vermont Act 128 V.S.A. § 4089e. Added 1997, effective April 27, 1998.

Administrative and Contractual Guidance

Benefit Determination Guidance

Prior approval is required and benefits are subject to all terms, limitations and conditions of the subscriber contract.

Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy. Benefits are subject to all terms, limitations and conditions of the subscriber contract.

Refer to the member's plan documents or outline of coverage for availability of benefits.
If the member receives benefits through a self-funded group, benefits may vary or not apply. To verify benefit information, please refer to the member's plan documents or contact the customer service department.

For New England Health Plan (NEHP) members an approved referral authorization is required.

Benefits for Federal Employee Program (FEP) members may vary. For further information please contact FEP customer service or refer to the FEP Service Benefit Plan Brochure.

Eligible Providers

Durable Medical Equipment
Network Pharmacy
Manufacturer

Audit Information

BCBSVT reserves the right to conduct audits on any provider and/or facility to ensure compliance with the guidelines stated in the medical policy. If an audit identifies instances of non-compliance with this medical policy, BCBSVT reserves the right to recoup all non-compliant payments.

Related Policies

Enteral Nutrition
Total Parenteral Nutrition
Nutritional Counseling

Policy Implementation/Update information

08/2000 new policy supersedes all prior policies concerning this benefit
05/2003 – removed case management requirement,
03/2005 updated, referral requirement removed for TVHP.
08/2006 modifier removed from HCPCS code
09/2007 annual review; minor wording changes to match current certificate language.
09/2008 annual review; benefit clarification made.
05/2009 annual review; no substantive change; approved by CAC
10/2011 Updated and transferred to new format. Vermont neonatal screening list updated. Official abbreviations and ICD-9 and ICD-10 codes for each condition added. Obsolete language referring to sources of formula removed. Added scientific references.
Medical/Clinical Coder reviewed 10/24/11 SAF
11/2013 (for 1/1/14 effective date) - Dollar limitation removed per VT State mandate requirement. Medical necessity criteria revised. ICD-10 remediated. Added diagnosis codes.

Scientific Background and Reference Resources

1. Rezvani I. Defects in metabolism of amino acids. Behrman RE, Kleigman RM, Jenson HB, editors. In: Nelson textbook of pediatrics. 17th ed. Philadelphia, PA: W.B. Saunders Company; 2004.p.398-433
2. Rezvani I. An approach to inborn errors of metabolism. Kleigman RM editor. In: Nelson textbook of pediatrics. 18th ed. Philadelphia, PA. Saunders. 2007.
3. The following website is useful to determine which products are assigned to a specific HCPCS code: https://www.dmepdac.com/
4. The following website was accessed 06/27/13: http://www.fda.gov/downloads/Food/ComplianceEnforcement/UCM073339.pdf
5.

Approved by BCBSVT Medical Directors **Date Approved**

Spencer Borden MD
Chair, Medical Policy Committee

Robert Wheeler MD
Chief Medical Officer

Attachment
ICD and CPT Code list

Code Type	Number	Brief Description	Policy Instructions
The following codes will be considered as medically necessary when applicable criteria have been met.			
HCPCS	S9434	Modified solid food supplements for inborn errors of metabolism	Prior Approval required
HCPCS	S9435	Medical foods for inborn errors of metabolism	Prior Approval required
HCPCS	B9998	Noc for enteral supplies	Prior Approval required
This policy applies to the following diagnoses codes only			
ICD-9	270.1	Phenylketonuria [PKU]	

ICD-9	270.2	Other disturbances of aromatic amino-acid metabolism (Tyrosinemia type I)	
ICD-9	270.3	Disturbances of branched-chain amino-acid metabolism (Maple syrup urine disease, beta-ketothiolase deficiency, isovaleric acid deficiency, methylmalonic acidemia, multiple carboxylase deficiency, propionic acidemia, 3-Methylcrotonyl-CoA carboxylase deficiency)	
ICD-9	270.4	Disturbances of sulphur-bearing amino-acid metabolism (Homocystinuria)	
ICD-9	270.5	Disturbances of histidine metabolism	
ICD-9	270.6	Disorders of urea cycle metabolism (Argininosuccinic acidemia, citrullinemia	
ICD-9	270.7	Other disturbances of straight chain amino-acid metabolism (3-OH 3-CH3 glutaric aciduria, Glutaric acidemia type I)	
ICD-9	270.8	Other specified disorders of amino-acid metabolism	
ICD-9	271.1	Galactosemia	
ICD-9	271.2	Hereditary fructose intolerance	
ICD-10	E70.0	Classical phenylketonuria	Effective 10/01/2014
ICD-10	E70.1	Other hyperphenylalaninemias	Effective 10/01/2014
ICD-10	E70.21	Tyrosinemia	Effective 10/01/2014
ICD-10	E70.5	Disorders of tryptophan metabolism	Effective 10/01/2014
ICD-10	E70.9	Disorder of aromatic amino-acid metabolism, unspecified	Effective 10/01/2014
ICD-10	E70.29	Other disorders of tyrosine metabolism	Effective 10/01/2014
ICD-10	E70.8	Other disorders of aromatic amino-acid metabolism	Effective 10/01/2014

ICD-10	E70.20	Disorder of tyrosine metabolism, unspecified	Effective 10/01/2014
ICD-10	E71.128	Other disorders of propionate metabolism	Effective 10/01/2014
ICD-10	E71.111	3-methylglutaconic aciduria	Effective 10/01/2014
ICD-10	E71.118	Other branched-chain organic acidurias	Effective 10/01/2014
ICD-10	E71.19	Other disorders of branched-chain amino-acid metabolism	Effective 10/01/2014
ICD-10	E71.110	Isovaleric acidemia	Effective 10/01/2014
ICD-10	E71.120	Methylmalonic acidemia	Effective 10/01/2014
ICD-10	E71.121	Propionic acidemia	Effective 10/01/2014
ICD-10	E71.0	Maple-syrup-urine disease	Effective 10/01/2014
ICD-10	E71.2	Disorder of branched-chain amino-acid metabolism, unspecified	Effective 10/01/2014
ICD-10	E72.12	Methylenetetrahydrofolate reductase deficiency	Effective 10/01/2014
ICD-10	E72.19	Other disorders of sulfur-bearing amino-acid metabolism	Effective 10/01/2014
ICD-10	E72.10	Disorders of sulfur-bearing amino-acid metabolism, unspecified	Effective 10/01/2014
ICD-10	E72.11	Homocystinuria	Effective 10/01/2014
ICD-10	E70.41	Histidinemia	Effective 10/01/2014
ICD-10	E70.40	Disorders of histidine metabolism, unspecified	Effective 10/01/2014
ICD-10	E70.49	Other disorders of histidine metabolism	Effective 10/01/2014
ICD-10	E72.22	Arginosuccinic aciduria	Effective 10/01/2014
ICD-10	E72.29	Other disorders of urea cycle metabolism	Effective 10/01/2014
ICD-10	E72.4	Disorders of ornithine metabolism	Effective 10/01/2014
ICD-10	E72.20	Disorder of urea cycle metabolism, unspecified	Effective 10/01/2014
ICD-10	E72.21	Argininemia	Effective 10/01/2014
ICD-10	E72.23	Citrullinemia	Effective 10/01/2014
ICD-10	E72.51	Non-ketotic hyperglycinemia	Effective 10/01/2014

ICD-10	E72.50	Disorder of glycine metabolism, unspecified	Effective 10/01/2014
ICD-10	E71.120	Methylmalonic acidemia	Effective 10/01/2014
ICD-10	E72.59	Other disorders of glycine metabolism	Effective 10/01/2014
ICD-10	E72.3	Disorders of lysine and hydroxylysine metabolism	Effective 10/01/2014
ICD-10	E72.8	Other specified disorders of amino-acid metabolism	Effective 10/01/2014
ICD-10	E72.03	Lowe's syndrome	Effective 10/01/2014
ICD-10	E74.20	Disorders of galactose metabolism, unspecified	Effective 10/01/2014
ICD-10	E74.21	Galactosemia	Effective 10/01/2014
ICD-10	E74.29	Other disorders of galactose metabolism	Effective 10/01/2014
ICD-10	E74.19	Other disorders of fructose metabolism	Effective 10/01/2014
ICD-10	E74.12	Hereditary fructose intolerance	Effective 10/01/2014
ICD-10	E74.11	Essential fructosuria	Effective 10/01/2014
ICD-10	E74.10	Disorder of fructose metabolism, unspecified	Effective 10/01/2014
Type of Service		Medical, DME supply	
Place of Service		Home	

Attachment II

Metabolic Disorder	Medical Food
Glutaric acidemia (GLA)	XLys, XTrp Analog XLys, XTrp Maxamaid XLys, XTrp Maxamum Glutarex-1 Glutarex-2 GA
Homocystinuria (HCU)	HCY1 HCY2 Hom2 Methionaid

	XMet Analog XMet Maxamaid XMet Maxamum Hominex-1 Hominex-2 HCU Gel HCU Express
Isovaleric acidemia (IVA)	XLeu Analog XLeu Maxamaid XLeu Maxamum I-Valex-1 I-Valex-2 LMD
Maple Syrup Urine Disease (MSUD) (Ketoaciduria)	BCAD1 BCAD 2 MSUD2 MSUD Analog MSUD Maxamaid MSUD Maxamum Acerflex Ketonex-1 Ketonex-2 Complex MSUD Complex Essential MSD MSUD Gel MSUD Express
Propionic acidemia (PPA) Methylmalonic acidemia (MMA)	OA1 OA2 OS2 XMTVI Analog XMTVI Maxamaid XMTVI Maxamum Propimex-1 Propimex-2 MMA /PA Gel MMA/PA Express
Phenylketonuria (PKU), Hyperphenylalaninemia	PhenylFree 1 PhenylFree 2 Phenyl-Free 2HP PKU1 PKU2 PKU3 XPhe Analog XPhe Maxamaid XPhe Maxamum

	Lophlex Periflex Phlexy-10 Phlexy-Vits Add-Ins Phenex-1 Phenex-2 PhenylAde PKU Gel PKU Express PKU Cooler Camino Pro
Sulfite Oxidase Deficiency	XMet, XCys Analog XMet, XCys Maxamaid
Tyrosinemia	TYROS 1 TYROS 2 Tyr2 XPhe, XTyr Analog XPhe, XTyr Maxamaid XPTM Analog Tyrex-1 Tyrex-2 TYR Gel TYR Express TYR Cooler
Urea Cycle Disorders (UCD) (Citrullinemia, Arginosuccinic Acidura)	WND 1 WND 2 UCD2 Essential Amino Acid Mix Cyclinex-1 Cyclinex-2
All Disorders(Protein Free Energy Modules)	PFD1 PFD2 Super Soluble Duocal Pro-Phree

[i] Vermont law Added 1997, No. 128 (Adj. Sess.), § 1, eff. April 27, 1998:
8 V.S.A § 4089e**. Treatment of inherited metabolic diseases.**