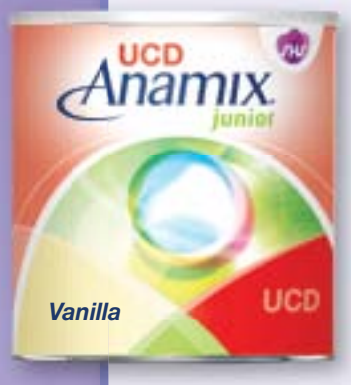

Guidelines for Management of Urea Cycle Disorders

A Practical Guide for the Use of UCD Anamix® Junior

Nutricia Learning Center
Specialized Nutrition Education – Helping You Help Your Patients

NUTRICIA
Metabolic Nutrition

Guidelines for Management of Urea Cycle Disorders:
A Practical Guide for the Use of UCD Anamix Junior

Table of Contents

UCD Anamix Junior is a medical food intended for use in dietary management of urea cycle disorders (UCD) in individuals over one year of age. The following guidelines are provided to help support healthcare professionals involved in the dietary management of UCD patients. Practices may vary from clinic to clinic, and this booklet should serve as guidance, not as strict protocol.

Acknowledgements

Nutricia North America would like to thank Sandy van Calcar, PhD, RD, University of Wisconsin at Madison, for her input and review of these guidelines.

Guidelines for the Management of Urea Cycle Disorders

INTRODUCTION AND BACKGROUND:

Basic Overview

The urea cycle is a group of six enzymes that are responsible for removal of waste nitrogen produced from the breakdown of amino acids. This nitrogen can be produced from exogenous (diet) sources or endogenous (catabolism) sources. The final product of the urea cycle is urea, which is a nontoxic compound excreted in the urine. In inborn errors of the urea cycle (UCD), urea is insufficiently produced and excess nitrogen is converted to ammonia instead. Inborn errors of metabolism have been described in all enzymes in the urea cycle.

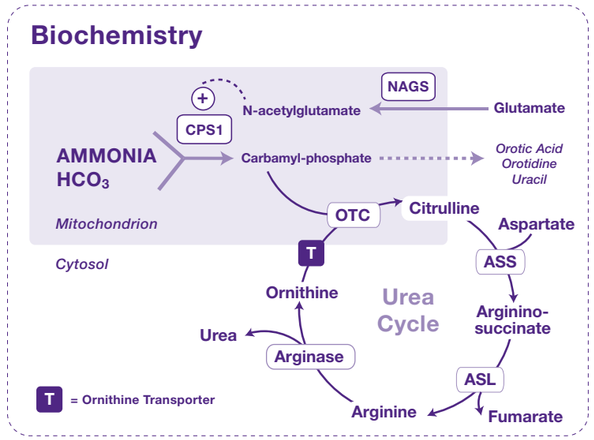

Figure 1. Metabolic Pathway[1] (to the right)

Table 1. Urea Cycle Disorders and corresponding enzyme defect

Disorder	Enzyme Defect
N-acetylglutamate synthetase (NAGS) deficiency	N-acetylglutamate synthetase
Carbamylphosphate synthetase 1 (CPS1) deficiency	Carbamylphosphate synthetase 1
Ornithine transcarbamylase (OTC) deficiency	Ornithine transcarbamylase
Citrullinemia type 1	Arginosuccinate synthetase (ASS)
Argininosuccinic aciduria	Argininosuccinate lyase (ASL)
Argininemia	Arginase
HHH syndrome (hyperammonemia, hyperornithinemia, homocitrullinuria)	Ornithine transporter defect (between cytoplasm and mitochondrion)

The hallmark feature in UCDs is **hyperammonemia**. Ammonia is extremely toxic to the central nervous system. Traditionally, urea cycle disorders were diagnosed with the onset of clinical symptoms caused by hyperammonemia. Clinical presentations of UCDs vary widely, depending on the disorder and the severity of the enzymatic defect. However, typical infantile presentations include poor feeding, lethargy, seizures, progressive encephalopathy, loss of reflexes, failure to thrive and ataxia. Later onset presentations can include chronic neurologic symptoms, behavioral problems, lethargy, psychosis and/or episodes of recurrent encephalopathy with high protein intake or illness[2]. Newborn screening by tandem mass spectrometry can detect citrullinemia, argininosuccinic aciduria and argininemia, although mild forms of these disorders may not be detected[3]. At this time, the other UCDs can only be detected in those presenting clinically or with a family history of the disorder.

1 Zschocke, et al. *Vademecum Metabolicum*. 3rd ed. Friedrichsdorf, Germany: Milupa GmbH&CoKG/Schattauer;2011:57
2 Visit the Urea Cycle Disorders Consortium Web site for information about the disorders, treatment guidelines, resources as well as UCD Registry. http://rarediseasesnetwork.epi.usf.edu/ucdc/
3 Visit www.ACMG.net for NBS ACT sheets and algorithms (Resource tab)

All UCDs are inherited in an autosomal recessive pattern, except for OTC deficiency which is an X-linked disorder. There is a wide range of phenotypes for the UCDs[4] . This is particularly true for OTC deficiency since women who are carriers of the OTC gene can present at any time during infancy through adulthood. Some women remain asymptomatic until a severe stress, such as the postpartum period following pregnancy and delivery[5].

Diet Principles

The urea cycle involves metabolism of all amino acids and thus, requires restriction in total protein intake. This approach to treatment is unlike PKU, MSUD, propionic and methylmalonic acidemia and other disorders of protein metabolism that require restriction of only one or more single amino acids. References 6 and 7 provide a detailed review of diet treatment for UCDs.

The three basic principles of UCD diet management include:

- Restriction of total protein intake through a combination of essential amino acids (EAA) and dietary (intact) protein to provide sufficient protein for normal growth and protein maintenance, while preventing excessive protein (nitrogen) intake, which may contribute to hyperammonemia due to a defective urea cycle.
- Provision of sufficient non-protein energy from dietary fat and carbohydrate to support growth and development, and spare use of protein as an energy source.
- Aggressively treat any illness or injury to either prevent or slow catabolism of body protein sources, which will increase the nitrogen load and may result in hyperammonemia.

Diet Prescription

The diet for those with UCD must be individualized for each patient. Many factors contribute to the protein tolerance of a patient including age, clinical status and the extent of the enzyme defect. The following steps apply to all prescriptions for UCD[6,7].

- **Establish patient's energy needs:** Table 2 (appendix) provides ranges for energy requirements for different ages. Standard methods can be used to determine caloric requirements, but it is important to use a patient's ADJUSTED BODY WEIGHT for calculations. This is particularly true for infants and growing children. Failure to thrive may be present with these disorders if inadequate energy intake is prescribed. Additional caloric needs may be needed during illness to account for fever, sepsis or other clinical complications[8].

- **Establish the patient's total protein needs:** Table 2 (appendix) provides a range of protein requirements for different ages. Typically, the DRI is used to establish a starting point for protein needs and then further adjustments are based on clinical status, nutrition assessment, growth and lab monitoring. Again, for those with poor growth, using the adjusted body weight is best for these calculations.
  NOTE:
  > For a child with poor weight gain, using actual weight may lead to underestimation of protein needs.
  > Patients with more severe enzyme defects may require a total protein intake below the DRI for age.
  > Use of essential amino acids such as those found in UCD Anamix® Junior or Essential Amino Acid Mix® allows for optimum protein utilization at lower protein intakes.[9]
- **Determine the distribution of protein:** For chronic treatment of a healthy patient, a distribution of 50% of total protein needs from essential amino acids and 50% from intact protein from food sources is a typical distribution. For older individuals, a lower percentage of total protein needs from essential amino acids may be appropriate.
- **Fluid Intake:** Calculate fluid intake based on standard recommendations for age. See Table 2 for guidance or ADA Pocket Guide[8].

4 Tuchman M, et al. Cross-sectional multicenter study of patients with urea cycle disorders in the United States. *Mol Genet Metab.* 2008 Aug;94(4):397-402.
5 Mendez-Figueroa H, et al. Management of ornithine transcarbamylase deficiency in pregnancy. *Am J Perinatol*. 2010 Nov;27(10):775-84.
6 Singh RH. Nutrition Management of Patients with Inherited Disorders of Urea Cucle Enzymes. In: *Acosta PB. Nutrition Management of Patients with Inherited Metabolic Disorders*. Sudbury, MA: Jones and Bartlett Publishers; 2010.
7 Singh RH. Nutritional management of patients with urea cycle disorders. *Inherit Metab Dis.* 2007 Nov;30(6):880-7
8 Refer to ADA Pocket Guide to Pediatric Nutrition Assessment. Latest edition available through Academy of Nutrition and Dietetics at www.eatright.org.
9 Acosta PB, et al. Nutritional therapy improves growth and protein status of children with a urea cycle enzyme defect. *Mol Genet Metab.* 2005:86(4):448-55

Managing the Diet

To meet essential amino acid requirements, intake of a medical food is often necessary. The composition of UCD Anamix Junior and Essential Amino Acid Mix are provided in tables 3 and 4 (appendix). Depending on the patient's age, add water to provide a caloric density of 20 to 30 kcal/fl oz. Divide the volume of UCD Anamix Junior or Essential Amino Acid Mix throughout the day.

Intake of intact protein sources from food MUST be carefully measured. Food composition resources are available for both families and professionals to provide accurate protein content for various foods and beverages. Use of nutrient composition information from food labels is often not accurate enough since protein content is rounded to the nearest gram.

Additional non-protein energy sources may need to be prescribed. Energy modules, such as Duocal™, can be added to UCD Anamix Junior or Essential Amino Acid Mix. Additional carbohydrate or fat-based foods or beverages can also be provided. Whether caloric intake needs to be counted is a patient-specific decision.

The following resources are available for families. Families should be instructed to use the columns for amount of food, protein and kilocalories.

- PKU Food List by Virginia Schuett (2010); www.pkunews.org
- PKU Food List by Emory University; contact Rosalynn Borlaza Blair, MA, Phone: (404) 778-8521; Email: rborlaz@emory.edu

For professionals, these resources can be helpful:

- Bowes and Church's Food Values of Portions Commonly Used. 19th ed. Lippincott Williams & Wilkins; 2010
- MetabolicPro diet analysis program (www.GMDI.org)
- USDA food composition tables (http://ndb.nal.usda.gov)

Supplementation of Other Amino Acids

With an enzymatic block in UCD, the product amino acid, distal to the enzyme block, becomes conditionally essential and must be supplemented in the diet. For those with CPS1 and OTC deficiency, either L-citrulline or L-arginine can be given at a dose of 100 – 170 mg/kg/d. Typically, L-citrulline is prescribed since additional nitrogen is used in the synthesis of arginine from citrulline. For citrullinemia Type 1 and argininosuccinic aciduria, L-arginine is given at a dose up to 700 mg/kg/d. **WARNING: Arginine should never be given to those with Arginase deficiency.**

Table 5. Suggested supplementation dosage of L-arginine and L-citrulline[7,10]

	L-Arginine	L-Citrulline
	mg/kg/d	mg/kg/d
CPS1 and OTC deficiency	100-170	100 - 170
ASS and ASL deficiency	up to 700	

10 Leonard JV. The nutritional management of urea cycle disorders. *J Pediatr.* 2001 Jan;138(1 Suppl):S40-4;discussion S44-5.

Monitoring

Monitoring is an essential part of UCD treatment as frequent adjustments to the diet are necessary to balance growth and adequate nutrition with metabolic control to prevent hyperammonemia.

The following markers should be included in a UCD monitoring plan. However, check your clinic policy:

- Growth parameters, including weight for height and body mass index (BMI) for those over age 2. Use caution when interpreting weight for height or BMI since these indices can be normal in those with both poor height and weight. See www.cdc.gov/growthcharts for growth charts.
- Serum ammonia. With effective treatment, concentrations of ammonia can be normalized for the majority of patients during times of health. However, proper handling of the blood sample is needed to prevent falsely elevated concentrations[11].
- Plasma amino acid profile. Depending on the disorder, concentrations of various amino acids are monitored, as listed in Table 6 below. The severity of the disorder influences the ability to normalize these concentrations and goals for therapy need to be individualized. Specific attention should be paid to the level of branched-chain amino acids particularly in patients receiving Na-phenylbutyrate drug therapy[12].
- Indices of protein status. Albumin, prealbumin (transthyretin), total protein and essential amino acids levels from a plasma amino acid profile are often used to assess overall protein status[7,8].
- Nutrition status. Various markers of nutrition status need to be routinely monitored. Diet record analysis for macro- and micronutrient intake is also recommended[8].

Table 6. Amino Acids to Monitor in Various UCDs[1]

Frequent monitoring is essential. Adjust diet accordingly to avoid excessive protein restriction. The following target values are guidelines only. Check with your clinic and lab guidelines.

Parameter	Value
Serum Ammonia (NH3)	<80 µmol/L
Urine Orotic Acid	<10 µmol/mol creatinine
Glutamine	<800 µmol/L
Arginine	80-150 µmol/L
Essential Amino Acids	should be in normal range
Isoleucine	>15 µmol/L
Threonine	> 100 µmol/L

Note: Orotic acid is only a useful marker for CPS1 and OTC deficiency. Isoleucine and threonine can be used as general markers of adequate protein intake.

When evaluating labs, diet adjustments need to be individualized for each patient. Typically, protein intake is increased or decreased in 10% increments. Labs are repeated in 3 to 7 days before further adjustments are made. It is essential to consider energy intake when making diet changes. If energy intake is insufficient, catabolism can cause elevated ammonia and amino acid concentrations.

11 Barsotti RJ. Measurement of ammonia in blood. *J Pediatr.* 2001 Jan;138(1 Suppl):S11-9;discussion S19-20.
12 Scaglia F. New insights in nutritional management and amino acid supplementation in urea cycle disorders. *Mol Genet Metab.* 2010;100 Suppl 1:S72-6.

Illness, Surgery or Injury: General Principles

Any illness, injury or surgical procedure is a catabolic event that can result in breakdown of body protein stores and contribute to hyperammonemia. Any of these events need to be taken seriously as metabolic decompensation can develop quickly and can be life-threatening. The entire metabolic team needs to work with families and individuals to plan for these events.

An emergency protocol should be provided to all caretakers and individuals with a UCD (see New England Consortium Website http://newenglandconsortium.org/). The content and complexity of the protocol can vary, but at a minimum should include patient demographics, diagnosis, immediate medical needs and contact numbers for a metabolic specialist. A medical bracelet or necklace is also recommended, especially for older children, adolescents and adults who may be away from caregivers who know about their UCD disorder.

Often, an at-home "sick-diet" is prescribed for those with UCDs. Sick-diet protocols need to be individualized. The patient's age and severity of his/her disorder will dictate the use of a sick-diet – perhaps it will be used only for a short-time during travel to an emergency facility or perhaps it is a protocol that can be utilized at home during periods of less severe illness.

If a patient can remain at home, general principles for designing sick-diets include:

- Increase non-protein energy sources from carbohydrate and fat. Non-protein energy sources should at minimum, meet baseline needs. Often additional energy is necessary to account for added needs of fever and illness processes. Use of stress factors utilized in nutrition support can be a helpful guideline[8].

Since monitoring protocols may vary:

- Providing sufficient energy intake is essential to help slow endogenous protein catabolism and inhibit hyperammonemia.
- Decrease dietary protein intake. The extent of reduction varies with the degree of illness, but is usually ≤ 50% of the patient's total protein prescription. Often food protein sources are removed with essential amino acids intake from medical food preserved or reduced. Elimination of all protein sources may be necessary in severe illness or catabolic processes. However, complete elimination of protein sources longer than 48 to 72 hours is not recommended since this can exacerbate protein catabolic processes[6]. Follow clinic guideline and protocol.
- Frequent small feeds and prevention of excessive fasting needs to be emphasized.

Families and patients should be instructed to contact their metabolic team any time a sick-diet is started. Guidance for medical management, lab monitoring and diet adjustments require individualization.

Illness: Admissions

When admissions are required, all protein sources are often initially removed from the diet. Providing an immediate source of non-protein calories is needed and peripheral or central IV access may be required to provide dextrose and lipid sources. Continued elimination of protein beyond 48-72 hours is not recommended since catabolism of endogenous protein sources can lead to increased ammonia and offending amino acids. When a protein source is restarted, UCD Anamix Junior can be given at an initial dose of 25 to 50% of the patient's usual protein prescription[6,7]. Incremental increases in protein are based on lab monitoring and clinical status. If necessary, nasogastric or other enteral feeding can be utilized until oral intake is possible. Case 1 illustrates an admission of a 2 year old girl with OTC deficiency.

Medication Used for Urea Cycle Disorders

Especially in severe UCDs, nitrogen-scavenger medications are an important adjunct to diet for treatment[13]. For hyperammonemic episodes, IV sodium phenylacetate and sodium benzoate (Ammunol™) is given with IV L-arginine. Administration requires central line access. For chronic management, sodium phenylbutyrate (Buphenyl™) can be administered orally. Both of these medications are distributed by Ucyclyd Pharma, Scottsdale, AZ (http://ureacycle.com). For those treated with nitrogen-scavenger medications, lower serum concentrations of the branched-chain amino acids (BCAA) leucine, isoleucine, valine have been reported and may require additional supplementation[14]. UCD Anamix Junior is supplemented with additional BCAAs to help support normal serum concentrations. Monitor serum BCAA concentrations as part of the patient's routine amino acid panel.

13 Batshaw MS, et al. Alternative pathway therapy for urea cycle disorders: Twenty years later. *J Pediatr.* 2001 Jan;1381(1 Suppl):S-46-54; discussion S54-5.
14 Scaglia F, et al. Effect of alternative pathway therapy on branched chain amino acid metabolism in urea cycle disorder patients. *Mol Genet Metab.* 2004;81 Suppl1:S79-85.

CASE STUDIES:
A 2-year-old girl with OTC deficiency

(Note: Case report as an example of diet calculation only.)

This patient presented in the emergency room with vomiting and overwhelming lethargy associated with a febrile illness. Her history includes four previous admissions at her local hospital with similar, but less severe symptoms. Her parents report that she has periods where she is “wobbly, glassy-eyed and combative”. She is a very picky eater and her weight gain has been poor, especially over the past 6 months.

Her ammonia level at admission was elevated at 350 µmol/L. Plasma amino acids show an elevated glutamine level and low citrulline and arginine concentrations suggesting a diagnosis of a urea cycle disorder. A central line is placed and Ammunol™ and L- arginine were initiated. Non-protein calories were started at 100 kcal/kg using 20% dextrose and 20% lipid IV solutions. Further testing found elevated orotic acid in urine, suggesting a diagnosis of OTC deficiency.

After 36 hours, her ammonia level decreased below 80 µmol/L and UCD Anamix Junior was initiated by NG tube to provide essential amino acids at 0.25 g/kg. Over the next week, protein was incrementally increased – first with UCD Animix Junior and then intact protein sources were added as oral intake improved. Total energy was held constant at 100 kcal/kg with gradual reduction in IV rate as her energy intake from medical formula and oral intake improved.

Based on weight gain and lab monitoring, the following were her diet goals at discharge:

	Prescription Goal per kg Body Weight	Total Prescription Goal (10.9 kg Body Weight)
Protein	1.6 g/kg/d	17 g/d
Energy	90 kcal/kg/d	950 – 1000 kcal/d

100 g UCD Anamix Junior provide 12 g protein equivalents (PE) and 385 kcal.

- **Determine total energy** prescription at 90 kcal/kg/d:
  90 kcal x 10.9 kg = 980 kcals. A calorie range of 950 to 1000 kcal/day is appropriate.
- **Determine total protein** at 1.6 g/kg/d: 0.8 g/kg from essential amino acids and 0.8 g/kg from intact protein
  10.9 kg x 0.8 g/kg = 8.7 g PE (both essential amino acids and intact protein are prescribed for a total of 17 g)
  Protein from medical food: 8.4 g PE = 70 g UCD Anamix Junior = 270 kcal
  Protein from natural food: 17 g – 8.4 g = 8.6 g. A range of 8 to 9 g protein/day is prescribed.
- **To meet energy needs**, 35 g Duocal (= 172 kcal) is added to UCD Anamix Junior in a total volume of 18 fl oz (24 kcal/fl oz). This is divided in 3 feedings/day.
- **Determine energy from natural food:**
  Energy: 1000 kcal – (270 kcal from UCD Anamix + 172 kcal from Duocal) = 560 kcal

	From UCD Anamix Junior (70 g)	From Duocal (35 g)	From normal food	Total
Protein (Equivalent)	8.4 g	0	8.6 g	17 g
Energy	270 kcal	172 kcal	560 kcal	1000 kcal

Initial plans after discharge include weekly monitoring of ammonia and plasma amino acids; weight is checked every 2 weeks.

CASE STUDIES:
A boy with ASA deficiency

(Note: Case report as an example of diet calculation only.)

This patient is an 8-year-old boy diagnosed with ASA deficiency soon after birth with a peak ammonia level of 520 µmol/L. He is developmentally delayed and a g-tube was placed at 9 months of age because of poor oral intake. Over the years, his oral intake improved and now the g-tube is used primarily for his medical food. Mom would like him to learn to drink his “milk”. His metabolic control is good on his current diet prescription:

- **Weight** = 23 kg; Height = 124 cm
- **Kcal needs** = 1600/day based on EER with active physical activity factor
- **Protein needs** = 1.0 g/kg; 0.5 g/kg from essential amino acids and 0.5 g/kg intact protein

His current medical formula provides 650 kcals and 12 g protein from essential amino acids.

He likes to drink Rice Milk from a cup, so a plan was developed to gradually add UCD Anamix Junior to rice milk for oral feeding. G-tube feedings will be gradually decreased as oral intake increases. To maintain a consistent intake, parents are instructed to use the g-tube for any medical food not consumed orally.

	Kilocalories	Protein – Essential amino acids	Protein - Intact
UCD Anamix Junior, 100 g	385	12 g	0 g
Rice milk, 18 fl oz + 4 fl oz water for 30 kcal/fl oz dilution	270	0 g	2.3 g
Food	900 to 1000	0 g	10 g

Appendix

Table 2. Guidelines for Protein, Energy and Fluid Intake for UCD patients.[14]

Age	Protein	Energy	Fluid
Infants	**g/kg**	**kcal/kg**	**mL/kg**
0 - 3 mo	2.20 - 1.25	150 - 125	160 -130
3 - 6 mo	2.00 -1.15	140 - 120	160 - 130
9 - 12 mo	1.60 - 0.90	120 - 110	130 -120
Girls and Boys	**g/d**	**kcal/d**	**mL/d**
1 - 4 years	8 - 12	945 -1890	945 -1890
4 - 7 years	12 - 15	1365 - 2415	1365 -2245
7 - 11 years	14 - 17	1730 - 3465	1730 -3465
Women			
11 - 15 years	20 - 23	1575 -3150	1575 -3150
15 - 19 years	20 - 23	1260 -3150	1260 -3150
> 19 years	22 - 25	1785 -2625	1875 -2625
Men			
11 - 15 years	20 - 23	2100 -3885	2100 -3885
15 - 19 years	21 - 24	2200 -4095	2200 - 4095
> 19 years	23 - 32	2625 - 3465	2625 - 3465

14 RDCRN, UCD Consortium; Urea Cycle Disorders Treatment Guidelines. Available at http://rarediseasesnetwork.epi.usf.edu/ucdc/physicians/guidelines-main.htm. Accessed April 3, 2012.

Table 3. Nutrition Information UCD Anamix Junior

NUTRITION INFORMATION		Per 100g	Per 10 g Protein Equivalent			Per 100g	Per 10 g Protein Equivalent
Energy	kcal	385	321	**Vitamins**			
Protein Equivalent	g	12	10	Vitamin A	mcg RE	960	800
Fat	g	17	14.2		IU	3197	2664
Saturated	g	1.9	1.6	Vitamin D_3	mcg	23	19.2
Monounsaturated	g	10.8	9		IU	920	767
Polyunsaturated	g	3.5	2.9	Vitamin E	mg α TE	18.5	15.4
Carbohydrate	g	46	38.3		IU	27.5	22.9
Linoleic Acid	mg	2786	2322	Vitamin K_1	mcg	92.2	76.8
				Thiamin	mg	1.9	1.6
Amino Acids, g				Riboflavin	mg	1.5	1.3
L-Cystine		0.43	0.36	Vitamin B_6	mg	1.5	1.3
L-Histidine		0.51	0.43	Vitamin B_{12}	mcg	3.8	3.2
L-Isoleucine		2.26	1.88	Niacin	mg	9.6	8
L-Leucine		3.82	3.18	Folic acid	mcg	461	384
L-Lysine		1.92	1.6	Pantothenic Acid	mg	6.1	5.1
L-Methionine		0.4	0.33	Biotin	mcg	34.6	28.8
L-Phenylalanine		0.67	0.56	Vitamin C	mg	120	100
L-Threonine		1.59	1.33	Choline	mg	480	400
L-Tryptophan		0.48	0.4	Inositol	mg	108	90
L-Tyrosine		1.23	1.03				
L-Valine		2.29	1.91	**Minerals**			
L-Carnitine		0.009	0.008	Calcium	mg	1555	1296
Taurine		0.069	0.058	Phosphorus	mg	1555	1296
				Magnesium	mg	246	205
				Iron	mg	26.9	22.4
				Zinc	mg	21.1	17.6
				Manganese	mg	3.6	3
				Copper	mcg	1900	1583
				Iodine	mcg	276	230
				Molybdenum	mcg	63.4	52.8
				Chromium	mcg	41.3	34.4
				Selenium	mcg	76.8	64
				Sodium	mg	1114	928
				Potassium	mg	1613	1344
				Chloride	mg	864	720

Table 4. Nutrition Information Essential Amino Acid Mix

Nutrient	Per 100 g	Per 10 g Protein Equivalent
Calories	316	40
Protein Equivalent	79	10
Fat, g	none	none
Carbohydrate, g	none	none
Amino Acids, g		
L-Cystine	3.78	0.48
L-Histidine	3.78	0.48
L-Isoleucine	10.4	1.32
L-Leucine	16.17	2.05
L-Lysine	13.25	1.68
L-Methionine	3.78	0.48
L-Phenylalanine	5.67	0.72
L-Threonine	11.35	1.44
L-Tryptophan	2.36	0.30
L-Tyrosine	9.46	1.20
L-Valine	14.56	1.84

Resources

- Zschocke J, Hoffmann GF. Vademecum Metabolicum. Friedrichsdorf, Germany. Milupa Metabolics/Schattauer; 2011. Available at Nutricia North America by calling 1-800-365-7354 (option 2 for Nutrition Services Department).
- Acosta PB. Nutrition Management of patients with Inherited Metabolic Disorders. Sudbury, MA. Jones and Bartlett Publishers; 2010.
- PKU Food List by Virginia Schuett 2010; www.pkunews.org.
- Singh RH. Nutritional Management of Urea Cycle Disorders. A Practical Reference For Clinicians. Emory University, Department of Human Genetics 2006 (booklet).
- Singh RH et al. Nutritional Management of Urea Cycle Disorders. Inherit Metab Dis. 2007 Nov; 30(6):880-7.
- PKU Food List by Emory University; contact Rosalynn Borlaza Blair, MA, Phone: (404) 778-8521; Email: rborlaz@emory.edu.

Websites

- **Ucyclyd Pharma:** http://ureacycle.com
- **National Urea Cycle Disorders Foundation:** http://www.nucdf.org
- **Urea Cycle Disorders Consortium:** http://rarediseasesnetwork.epi.usf.edu/ucdc
- **MetabolicPro diet analysis program:** http://www.GMDI.org
- **USDA Food Analysis Program:** http://ndb.nal.usda.gov

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